THE UNIVERSITY OF ALBERTA

1. ON THE MECHANISM OF CHLORINATION BY N-CHLOROAMINES
2. ON THE MECHANISM OF BROMINATION BY N-BROMOSUCCINIMIDE

BY

(C) CHRISTIAN P. MEINTZER

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled

ON THE MECHANISM OF HALOGENATION WITH

N-HALOAMINES OR N-HALOIMIDES

submitted by CHRISTIAN P. MEINTZER in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

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Date March 2, 1984

To my wife, Judy, and to Stephen.

For patience and understanding.

ABSTRACT

PART 1

The photochlorinations of the n-butyl, n-pentyl, and n-hexyltrimethylammonium chlorides, using molecular chlorine in hexachloroacetone or 15% CD_3CO_2D/85% H_2SO_4, or using N-chlorodimethylamine in the acid solvent are described. The ammonium group exerted a strong polar directing effect upon the site of substitution. This effect was found to be more pronounced in the more polar protic solvent. The reagent, N-chlorodimethylamine, generated the dimethylamminium radical, whose reaction showed a polar sensitivity toward hydrogen abstraction similar to that of the chlorine atom, but exhibiting a much greater selectivity. Comparison of the isomer distributions obtained from the self photochlorination reactions of N-chloro-n-hexylmethylamine and N-chloro-n-pentylmethylamine in the acid solvent, with the distribution pattern obtained for the chlorinations of the ammonium salts with N-chlorodimethylamine, suggested that the self chlorinations of the N-chloroamines proceed by the intramolecular hydrogen abstraction mechanism suggested previously.

PART 2

The competitive N-bromosuccinimide (NBS) brominations of cyclopentane vs. cyclohexane, or neopentane vs. dichloromethane were shown to proceed by a mechanism dominated by either a bromine atom chain, a succinimidyl radical (NS·) chain, or a mixed chain. The dominance of each of the major chain-carrying processes depends upon the solvents used, to some degree upon the reactivity of the substrate, and upon the additives (molecular bromine or olefin) used to moderate or enhance one or the other of the chain processes.

A low value, ~0.05, of the relative rate of reaction/H, r, with neopentane vs. dichloromethane was determined for the bromine atom chain, while a high value, r ~19, was observed for the succinimidyl radical chain. Intermediate values of r could be obtained by carrying out the reactions to varying percentages of reaction, since as the reaction proceeded the importance of the bromine atom chain becomes more prominant.

Accompanying the abstraction reaction of the succinimidyl radical, a ring opening process occurs, which led, by a chain sequence, to the production of β-bromopropionyl isocyanate (β-BPIC). The amount of ring opened product could be controlled by the concentration of

bromine present in solution, since the succinimidyl radical reacts rapidly with molecular bromine, preventing its further reaction. For the reactions with neopentane and dichloromethane the fractional amount, $X_{NS\cdot}$, of abstraction by NS· could be determined from the observed r values. Since ring opened product was observed in all reactions, the fraction of abstraction/ring opening, $X_{NS\cdot}/[\beta\text{-BPIC}]$, could be measured and was found to be a constant regardless of the value of r obtained.

Addition of more reactive substrates, or olefinic materials to the reaction mixtures containing NBS in dichloromethane with added olefin (the reaction conditions previously reported) yielded heterogeneous mixtures of NBS and substrate. The reactions showed a constant ratio of products, $[BrCHCl_2]/[\beta\text{-BPIC}]$, (contrary to a previous report).

The addition of benzene was found to serve as a succinimidyl radical trap, allowing a competitive abstraction between bromine atoms and succinimidyl radicals, and leading to a larger ratio of products, $[BrCHCl_2]/[\beta\text{-BPIC}]$. Reactions run in solvent chloroform were found qualitatively to behave the same as experiments carried out in dichloromethane, contrary to a previous report.

Large yields of β-IPIC were found to be produced in

the reactions of N-iodosuccinimide with iodine in solvents dichloromethane or chloroform. These reactions were assigned, tentatively, to the reactivity of complex radicals.

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PART 1

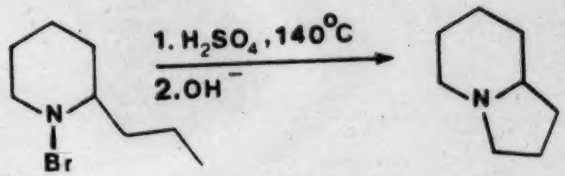
INTRODUCTION

I.1 Background

The acid-catalyzed chlorination reactions of N-haloamines have been studied extensively. The reactions can be divided into two groups, those involving intramolecular hydrogen abstraction and those involving intermolecular hydrogen abstraction. The intramolecular analog of the halogenation, known as the Hofmann-Löffler-Freytag reaction,[1] has been used extensively in the syntheses of a variety of nitrogen containing heterocyclic compounds.[1-16] In the intramolecular reactions the N-chloroamine undergoes an initiated self chlorination reaction and the product mixture is usually treated with base, without isolating the intermediate halide. Intramolecular cyclization yields five or six membered ring heterocyclic products arising from nucleophilic substitution of the halogen by the free amine. The intermolecular reactions have used N-chloroamines as reagents to produce a variety of selectively halogenated compounds which do not contain an amine functional group.

The first example of the intramolecular reaction was observed by Hofmann[9,17] in 1885 during treatment of N-bromoconiine (1) with hot sulfuric acid. A tertiary

amine was formed and shown to be δ-coneceine (2).[10]



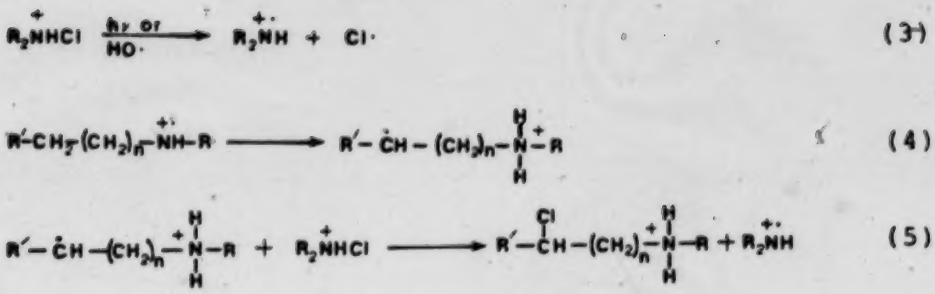
1 2 (1)

Löffler, Freytag and Kober[18-20] extended the method to several other examples, one of which included the synthesis of nicotine (4) from the N-bromoamine (3).[19]

3 4 (2)

The results of numerous other studies were reported between 1910 and 1960 and these are well documented in a review by Wolff.[1]

The first study of the mechanism of the reaction was reported by Wawzonek, Thelen and Nelson in 1950.[8,21] They found the reaction to be catalyzed by irradiation or hydrogen peroxide and on this basis proposed a free radical chain mechanism (see Scheme I).



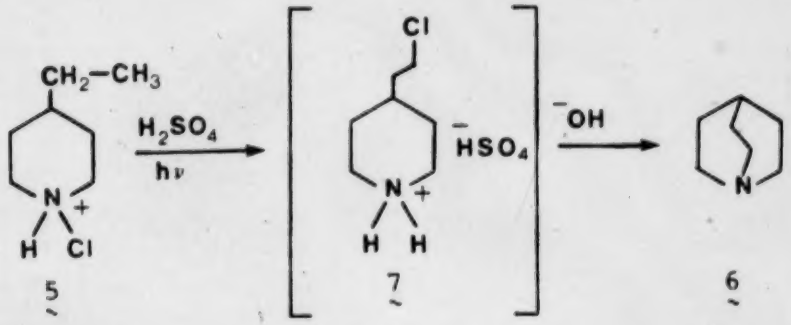
(3)

(4)

(5)

Scheme I

These workers also studied the reaction of N-chloro-4-ethylpiperidine (5) in sulfuric acid under irradiation with ultraviolet light.[21] The acid solutions were slowly neutralized and adjusted to pH 9, after which the pH was found to drop to 5. Quinuclidine (6) was isolated from



(6)

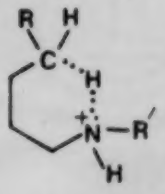
this solution. On the basis of the observed change in pH, 4-(β-chloroethyl)-piperidinium salt (7) was proposed to be an intermediate in the reaction, which is converted to the free amine by base, which then cyclizes to quinuclidine.

Corey and Hertler confirmed these conclusions and

extended the understanding of the mechanism with their study in 1960.[3] (-)-N-chloromethylamylamine-4-d was decomposed in sulfuric acid at 95°, and optically inactive, partially deuterated, 1,2-dimethylpyrrolidine was obtained in 43% yield. This was considered to be strong evidence for a radical intermediate since a trigonal carbon center is required for racemization. The deuterium content of the 1,2-dimethylpyrrolidine was measured. An isotope effect (k_H/k_D) of 3.54 indicated that considerable breakage of the carbon-hydrogen bond occurred in the rate determining step. N-chloro-n-butyl-n-butyl-4-d_3-amine was also cyclized, and, on the basis of the ratio of dideuterated product to trideuterated product, an isotope effect of 2.6 was calculated. Ultraviolet irradiation, sweeping with nitrogen, and addition of ferrous ion were all found to catalyze the intramolecular cyclization reactions. When the reactions were carried out in mixtures of acetic acid/sulfuric acid the rate of reaction was found to be dependent upon the concentration of sulfuric acid, with no reaction occurring in glacial acetic acid.

In 1965 Neale and Walsh studied the effect of the concentration of sulfuric acid on the rate of reaction, as well as the effect of the purity of the N-chloroamine, light intensity, light wavelength, and nitrogen

sweep rate.[22] Increasing acidity was shown to increase the yield of cyclic product, but decreased the overall reaction rate. Neale, Marcus and Walsh also studied the use of alternative acids as media for the radical promoted cyclizations.[23] Trifluoroacetic acid, sulfuric acid/nitromethane and sulfuric acid/acetonitrile were found to be acceptable alternative solvents for the reaction. Gassman and Heckert attempted to design a reaction substrate which would prefer abstraction of the γ-hydrogen rather than the δ-hydrogen.[13] The abstraction of the δ-hydrogen had been proposed to be favored because of the intermediacy of a six-membered transition state (8) and the preference for linear hydrogen abstraction.[3]



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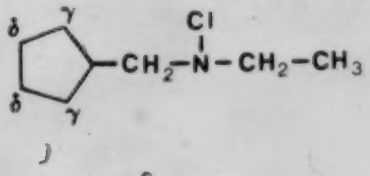

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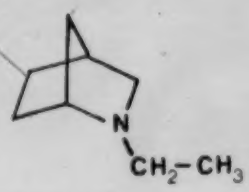
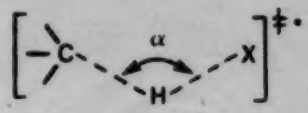


10

Cyclization of 9, however, yielded only the expected product of δ-abstraction 10. These observations were presented as evidence for the importance of the angle of hydrogen abstraction to the rate of the reaction. Abstraction of the δ-hydrogens is sterically less favorable than γ-hydrogen abstraction due to the greater

distance from the nitrogen center (2.2 Å for the δ-H and 1.8 Å for the γ-H), however, the abstraction angle α (see 11) for the δ-H transition state (145°) is closer to 180° than the angle (α) for the transition state leading to γ-H abstraction (120°), and the δ-substitution product is formed.



11

During an investigation of the amination of various substituted benzenes using N-chloroamines Minisci, Galli and Cecere[24] found that benzyl chlorides were produced as side products. They initiated a series of investigations of the intermolecular chlorination and bromination of various substituted alkanes using a variety of initiators in 85% H_2SO_4/15% CH_3CO_2H.[25-27] The reagents showed very high selectivities and the reactions using N-chloroamines gave similar selectivities to those using N-bromoamines. They also found the selectivity observed was dependent upon the initiator used, with cuprous salts giving the highest selectivity and ferrous salts giving the lowest selectivity. On the basis of the results, but contrary to the suggested change in selectivity with changing in-

itiator, they proposed the following mechanism (Scheme II):

$$(CH_3)_2\overset{+}{N}HCl + \overset{+}{M} \longrightarrow (CH_3)_2\overset{+\cdot}{N}H + \overset{+}{M}Cl \quad (7)$$

$$R\text{-}H + (CH_3)_2\overset{+\cdot}{N}H \longrightarrow R\cdot + (CH_3)_2\overset{+}{N}H_2 \quad (8)$$

$$R\cdot + (CH_3)_2\overset{+}{N}HCl \longrightarrow (CH_3)_2\overset{+\cdot}{N}H + R\text{-}Cl \quad (9)$$

Scheme II

Minisci reported a high selectivity for hydrogen abstraction at the second carbon of heptane (see below).[27] The selectivity at this carbon is almost

$CH_3\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}CH_3$
1.1 55.6 29 14.3

using Me_2NCl in H_2SO_4

double that at carbon three. He proposed that this high selectivity was caused by the steric bulkiness of the dimethylamminium radical, and that the second carbon is the least hindered secondary carbon. To test this proposal he also investigated the reactions of N-chlorodiisobutylamine, a bulkier reagent, to see if its selectivity would change (see below). He found an even greater selectivity

$CH_3\text{—}CH_2\text{—}CH_2\text{—}CH_2\text{—}CH_2\text{—}CH_2\text{—}CH_3$
1.3 64.4 22.9 11.3

using N-chloro-diisobutylamine in H_2SO_4

using this reagent and thus concluded the steric bulkiness of the N-chloroamine is responsible for the high

selectivity at the second carbon.

Neale and Gross in 1967 studied the relative reactivities of various ring substituted toluenes toward chlorination in $2MH_2SO_4/CH_3CO_2H$ with N-chloropiperidine.[28] The relative reactivities showed a satisfactory Hammett correlation (σ^+) $\rho = -1.36$. The ρ value obtained was much more negative than that for the chlorine atom ($\rho = -0.66$[29]), and thus was proposed to be the ρ value characteristic of a piperidinium radical.

In 1969 Tanner and Mosher[30] proposed that intermolecular hydrogen abstractions, executed with metal ion initiated N-chloroamines produced by the procedure of Coleman[2] (hereafter referred to as the synthetic method), did not occur via an amminium radical, but rather via a chlorine atom chain. They based this conclusion on several pieces of evidence. The chlorination of 1-chloropropane (Footnote 1) with molecular chlorine and with various N-chloroamines all gave the same isomer distribution of products. Ferrous sultate, ferrous chloride, and cuprous chloride initiated chlorinations

[1] The substrates chosen for study yielded products that were stable to the solvent H_2SO_4/CH_3CO_2H.

with the N-chloroamines all gave the same isomer distribution of products (identical to that obtained with molecular chlorine), and the relative reactivities of various hydrocarbons versus cyclohexane, to N-chlorodiethylamine and molecular chlorine, were shown to be the same. They pointed out that the similar results with the different initiators was to be expected, since Minisci's mechanism did not involve the metal salts in the hydrogen abstraction step. All of these results supported the involvement of a chlorine atom chain for these experiments. They proposed that, for several substrates previously studied, the differences in selectivities observed were shown to be due to instability of the products in the solvents used.

Minisci, Gardini and Bertini[31] responded with additional results obtained using 1-chlorobutane, 1-chlorohexane, methylpentanoate and methylheptanoate which they claimed to be stable to the H_2SO_4/CH_3CO_2H solvent. Reactions using N-chlorodimethylamine were found to give higher selectivies than those observed for molecular chlorine, and N-chlorodimethylamine and N-bromodimethylamine were found to give the same selectivities. Based on these results they reaffirmed their original conclusion that an amminium radical was the abstracting species involved.

The apparent discrepancy in the results obtained by these two groups was clarified by Spanswick and Ingold in 1970.[32] They found the important factor was the purity of the N-chloroamine. The N-chloroamines investigated were purified by precipitation from ether as the hydrosulphate salt. The crystalline salt was washed with ether, dried and dissolved in the solvent of choice. Reactions of N-chlorodimethylamine and N-chloropiperidine, purified in this manner, with 1-chlorobutane in $4M H_2SO_4/CH_3CO_2H$ gave isomer distributions clearly different from those obtained with molecular chlorine (see below).

Cl-CH_2—	—CH_2—	—CH_2—	—CH_3	
5.1	23.5	45.6	25.8	Cl_2, hν, 4M H_2SO_4/HOAc
4.8	10.6	78.8	5.8	Me_2NCl, 4% AIBN, 4M H_2SO_4/HOAc
4.9	10.1	78.6	6.4	$(CH_2)_5NCl$, 4% AIBN, 4M H_2SO_4/HOAc

Various initiators were used and found to give varying results. Ferrous sulphate, cerous sulphate, cerous chloride and cobaltous chloride were all found to yield results which were closer to those obtained from molecular chlorine. In all of these reactions the distinct odor of molecular chlorine was noted and thus was suggested to be the cause of the differing values obtained. This was proposed to be the cause behind the variation in values obtained by Minisci.[25]

They further showed that N-bromodimethylamine when purified as described for the N-chloroamines gave selectivities identical to N-chlorodimethylamine and different from those obtained using molecular bromine (see below). Based on these results they concluded that

$Cl-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_3$	
23.6	26.4	49.5	0.5	Br_2, hν, 4 M H_2SO_4 / HOAc
4.6	8.8	77.3	9.3	Me_2NBr, 10 % AIBN, 4 M H_2SO_4 / HOAc

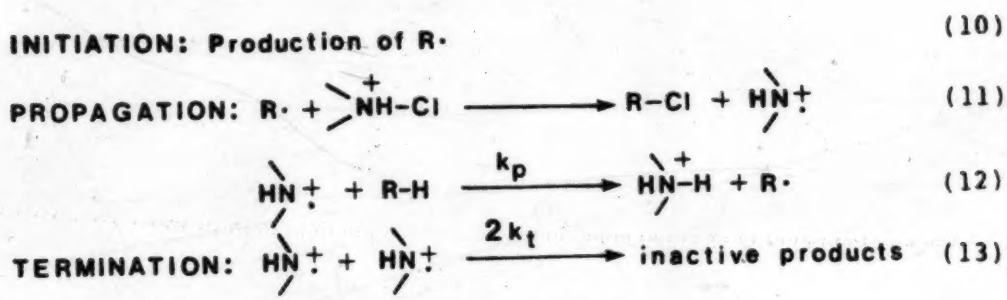
careful purification of the N-haloamine is important to achieve an amminium radical chain. The synthetic method was not considered to produce N-haloamines of sufficient purity to eliminate the participation of a molecular halogen chain.

Spanswick and Ingold also investigated the kinetics of the intermolecular reaction and measured several rate constants.[33] They measured the chain chlorination of decanoic acid by N-chlorodimethylamine and N-chloropiperidine in sulfuric acid/acetic acid at 30°. The induction period method did not work satisfactorily for estimation of the rate of chain initiation, since no suitable inhibitors could be found. Because of this problem, the rate of chain initiation had to be estimated from the measured rates of decomposition of α,α'-azobiscyclohexylnitrile (ACHN) and α,α'-azobisisobutyronitrile

(AIBN). The rotating sector method was used to determine the rate constants of propagation and termination. Using the limits of the estimated rate of initiation the rate constant of termination was estimated to be in the range 6×10^6 to 5×10^7 $M^{-1}s^{-1}$, and the rate constant for propagation was estimated to be in the range 7×10^2 to 1×10^4 $M^{-1}s^{-1}$.

The overall reaction rates were found to be proportional to the concentration of decanoic acid, the square root of the rate of chain initiation, and independent of the concentration of N-chloroamine. At any particular ACHN concentration the rates were proportional to the square root of the light intensity, which indicated the chains are terminated by the bimolecular reaction of two radicals. These results were all found to be consistent with the mechanism in Scheme III. Since however, they could not distinguish these rate constants from ones obtained for chlorine atoms, the establishment of the identity of the abstracting species, in the previous report,[32] was essential for their conclusions.

It was not possible for the authors to accurately predict the nature of the terminating radicals. Since the amino radicals are in equilibrium with the amminium radicals three possible terminations exist: amminium with amminium radical, amino with amminium radical, or



Scheme III

amino with amino radical. Even though the concentration of amminium radicals should favor the first possibility, the rate constants for the second and third examples would be expected to be much larger due to the absence of charge repulsion.

Three reviews of the chemistry of nitrogen cation radicals appeared in the early seventies. One, by Kovacic, Lowery and Field in 1970,[34] reviews the reactions of N-chloroamines and N-bromoamines with 317 references cited. The second, by Deno in 1972,[35] reviews the chemistry of nitrogen cation radicals. The third, by Minisci in 1973,[36] reviews novel synthetic applications and deals mainly with the amination of aromatic compounds, but contains a section on the intermolecular halogenation of saturated monofunctional alkanes.

Deno, Fishbein and Wyckoff[37] published the results of a study of the chlorination of carboxylic acids in

strongly acidic media with molecular chlorine. They reported high yields of chlorination products resulting from abstraction at the terminal methyl groups of the carboxylic acids. Subsequent to this first report on terminal functionalization, Deno and his co-workers published several studies investigating the possibility that steric effects influenced the hydrogen abstraction reactions of sterically bulky N-chloroamines. Minisci had first suggested this behavior in his study in 1968[27] to explain terminal methylenefunctionalization. Deno, in trying to mimic methylfunctionalization found in enzyme reactions,[38] investigated this idea further.

Deno and his co-workers observed high selectivity for abstraction from the methylene group furthest removed from the functional group (59-93% of yield) in the chlorination of alcohols, ethers, carboxylic acids, and amides with N-chlorodiisopropylamine in strong acid.[39] The reactions of the amines, unlike those of molecular chlorine, gave (ω-1) chlorination. A predominance of monochlorination (60-80%) was observed with the remainder being unchlorinated. This observation was rationalized as being due to the deactivation towards further hydrogen abstraction by the electronegative chloro substituent. They observed the same high selectivity in alkanes as well, in studies of their chlorination in strong acid by

N-chloroamines of varying steric bulk.[40,41] Using isopentane, 2,2-dimethylbutane, 2,3-dimethylbutane, 2-methylbutane, and pentane, the primary to secondary to tertiary hydrogen atom selectivities were measured for the N-chloro derivatives of dimethyl-, dicyclohexyl-, diisopropyl-, dineopentyl-, di-t-butyl-, t-butyl-t-amyl-amines and 2,2,6,6-tetramethyl piperidine. The N-chloro derivatives of di-t-butyl-, t-butyl-t-amylamines and 2,2,6,6-tetramethyl piperidine showed the largest primary to tertiary selectivities, with those of di-t-butyl- and t-butyl-t-amyl having selectivities >1:1 (~1.7:1, P:T). This high inverse selectivity was said to be due to the steric bulkiness of the abstracting N-chloroamines. The primary to tertiary selectivities were also seen to increase as the steric crowding of the tertiary hydrogens increased.

In 1975 Deno[42] retracted his results reported for the chlorination of carboxylic acids in strongly acidic media with molecular chlorine.[37] In a study of the stability of monochlorinated octanoic acids in >83% H_2SO_4 it was found that the C-5 to C-7 chlorinated compounds decomposed with half-lives in the range of the reaction times employed. Therefore their results which showed high selectivity for C-4 and C-8 chlorination were invalid. The product with the shortest half-life, was

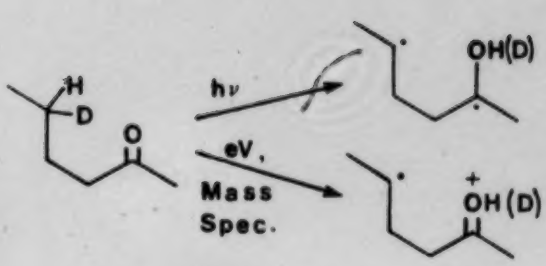
that chlorinated at C-7, and thus other work done in this range of sulfuric acid concentrations may have selectivities for abstraction from the methylene group furthest removed from the functional group which are in error, and should actually be greater still.

Because of this solvolytic problem a later study of Deno, Gladfelter and Pohl[43] involving the chlorination of pentane, hexane, octane, decane and dodecane was run in trifluoroacetic acid. A high selectivity was observed for chlorination at C-2 although dichlorination of octane, decane and dodecane was observed, making conclusions drawn from the product ratios for these compounds unreliable. Using 2,6-dimethylpiperidine, diisopropyl-, dicyclohexyl-, and 2,2,6,6-tetramethylpiperidine N-chloroamines to chlorinate decane, 2,2,6,6-tetramethylpiperidine was found to give the highest selectivity for C-2 chlorination.

Using N-chlorodiisopropylamine Deno and Jedziniak[44] chlorinated lauramide using 80% H_2SO_4/20% H_2O and palmitamide in 30% H_2SO_4/70% CH_3CO_2H. Since 88% of the chlorination occurred on C8-C10 for both amides, a novel explanation was invoked. Because of the hydrophobic nature of the long aliphatic chains Deno proposed that the carbon skeleton folds back on itself to minimize exposure to the solvent. When this is done, the positions furthest removed from the polar amido group are C8-

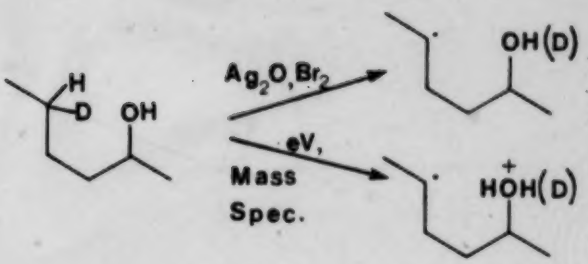
C10 and are thus the favored sites for hydrogen abstraction by the diisopropylamminium radical.

The McLafferty rearrangement observed in the mass spectra of ketones and alcohols is a similar reaction to the intramolecular Hofmann-Loffler-Freytag reaction. Both reactions have been proposed to involve a cyclic six-membered transition state for hydrogen abstraction by a cation radical. Green and co-workers[45] noticed a discrepancy in the literature between the k_H/k_D values obtained for abstraction at the γ-carbon of ketones and alcohols by mass spectroscopy, and those obtained by chemical and photochemical methods (see equations 14-17). They proposed that cation radicals are more energetic and thus exhibit smaller k_H/k_D than uncharged radicals. They suggested therefore, that the Hofmann-Loffler-Freytag reaction should also give a value of k_H/k_D close to one. The result they obtained was in agreement with this proposal (see equation 18). This result, however, is in conflict with the result obtained by Corey[3] (see equation 19). The difference may, however, only reflect a difference in the efficiency of the base promoted cyclization step. However, since Ingold showed the intermolecular analogs to be complicated by the incursion of a chlorine atom chain when Fe^{++} is used as the initiator, the difference may be due to a mixed chain.



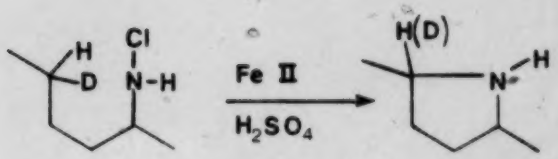
$k_H/k_D = 5.7$ (14)

$k_H/k_D = 1.1$ (15)

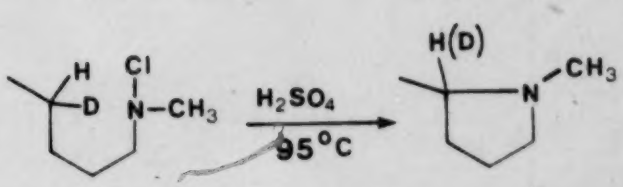


$k_H/k_D = 4.8$ (16)

$k_H/k_D = 1.1$ (17)



$k_H/k_D = 1.2$ (18)



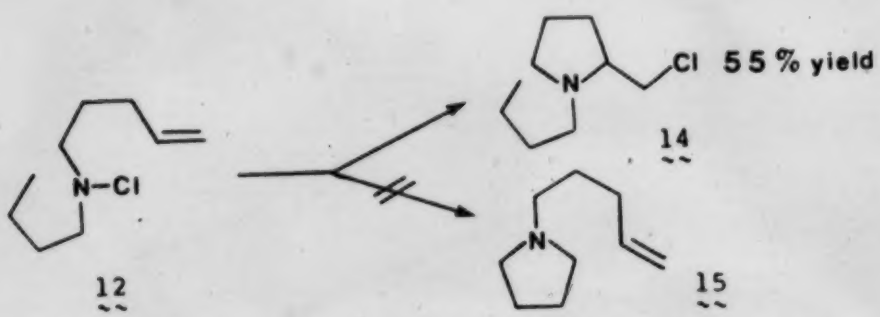
$k_H/k_D = 3.48$ (19)

An alternate explanation for this discrepancy would need to invoke differences in the extent of protonation of the two different nitrogen radicals studied (see equations 18 and 19).

Neale[46-50] and Minisci[51,52] both carried out extensive studies in the 1960's on the addition reactions of N-chloroamines to olefins. Neale studied the reactions of N-chloroamines which could either cyclize via the

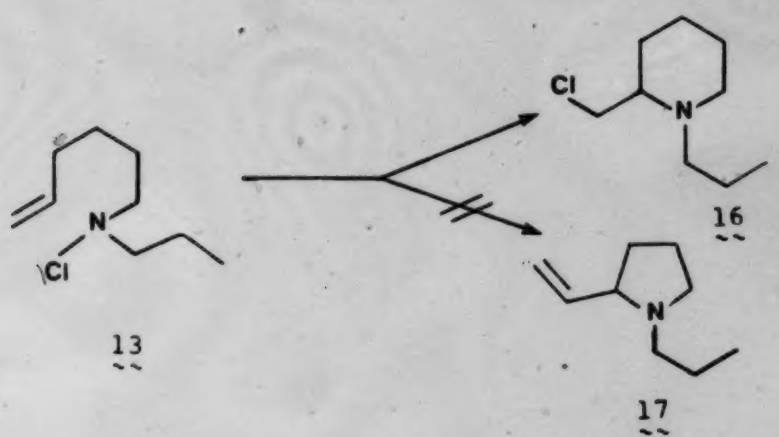
Hofmann-Loffler-Freytag reaction, or could undergo competitive addition to an added olefin substrate. Based on the results obtained, Neale concluded that the abstraction-cyclization reaction was highly favored over addition to the added olefin.[48] Surzur, Stella and Tordo[53] noted that Neale's studies always involved competition between an intramolecular cyclization and an intermolecular addition to the added olefin. This competition provides an entropy advantage to the intramolecular cyclization and thus may not be a true indicator of the preference of the amminium radicals. They investigated the behavior of N-n-butyl-4-pentenyl-N-chloroamine (12) and N-n-propyl-5-hexenyl-N-chloroamine (13) which can undergo an intramolecular reaction by the Hofmann-Loffler-Freytag reaction (hydrogen abstraction), or by addition to the olefin.

Compound 12 when initiated with a ferrous salt was shown to give only 2-chloromethyl-N-butypyrrolidine (14) the product of addition to the olefin and none of the Hofmann-Loffler-Freytag product, N-4-pentenylpyrrolidine



12 14 15

(15). This result is in contrast to that found by Neale, however entropy effects are now close to equivalent. Even compound 13 where the Hofmann-Loffler-Fretyag reaction would involve abstraction of an allylic hydrogen gave only product 16 and none of compound 17.



50% yield

13 16 17

Two examples exist, of the Hofmann-Loffler-Freytag cyclization, which involve different conditions from those normally employed. Schmitz, Schinkowski, and Murawski have obtained yields of 60 to 85% of pyrrolidines from primary N-chloroamines.[54] They also demonstrated that when the primary N-chloroamines are being prepared, either RNHCl or $RNCl_2$ could be the major product.[55] The second example is the work of Ban, Kimura, and Oishi[16,56] who reported the synthesis of nitrogen heterocycles in the absence of a strong acid catalyst. They developed a procedure for synthetic purposes in the absence of acid, and actually add triethylamine to trap the HCl produced. Using their

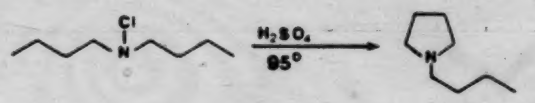
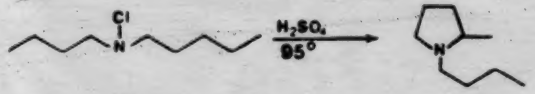
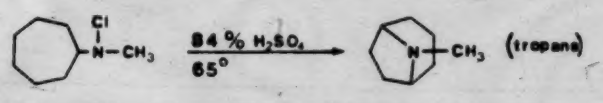
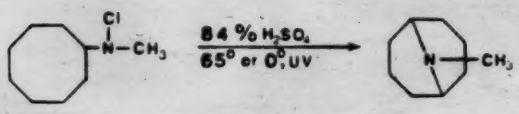
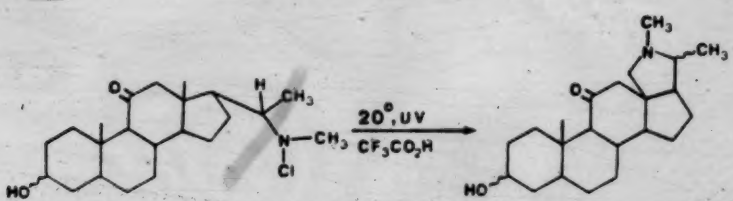
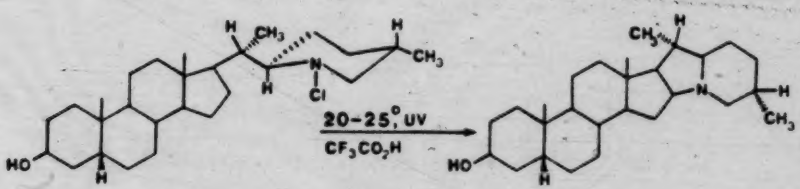
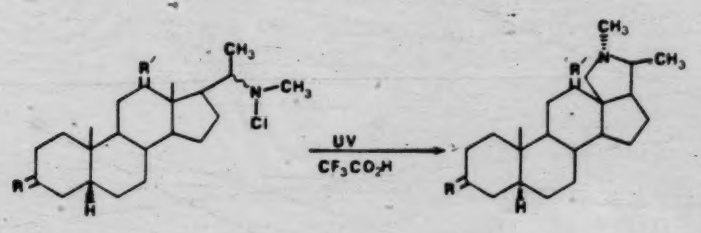
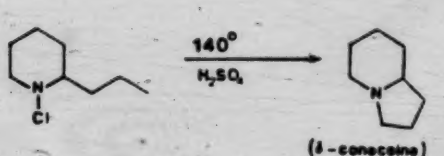
procedure they have obtained yields of 50 to 100%, based on starting N-chloroamine.

I.2 Proposal

Tanner and Mosher[30] showed that the intermolecular abstractions using N-chloroamines, when prepared by the synthetic procedure, give results consistent with a chlorine atom chain rather than an amminium radical chain. Ingold and Spanswick[32] later showed that N-chloroamines, carefully purified, can give results which are consistent with an amminium radical chain. The majority of the synthetic reactions which have been reported to utilize the intramolecular Hofmann-Löffler-Freytag reaction, however, have involved starting N-chloroamines which were prepared following the synthetic method.[2]

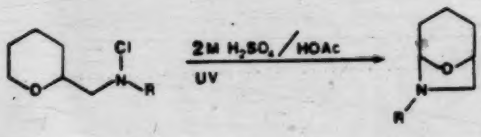
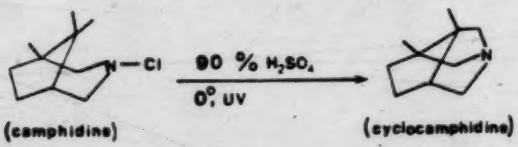
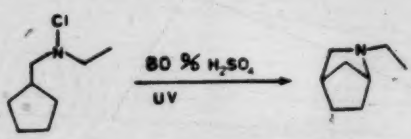
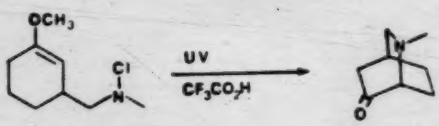
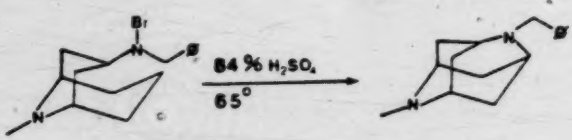
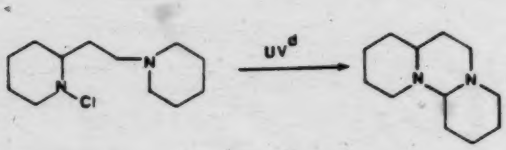
The intermolecular abstractions using N-chloroamines show very high selectivity with the yields of the major products being in the range 44 to 93 percent.[24-28,35,36,39-43] As can be seen in Figure 1, many of the products from supposedly intramolecular reactions are produced in much smaller yield. Because of the entropy advantage of an intramolecular abstraction over an intermolecular abstraction, product yields would be expected to be as high or higher for the intramolecular

Figure 1. Some Synthetic Examples of the Hofmann-Löffler-Freytag Reaction.

Example[a]	% Yield	Reference
	70	2
	35	3
 (tropane)	40	4
	23	5
	85	6
	37	7
	3-39[b]	8
 (δ-conacaine)	40	9,10

continued...

Figure 1 (continued):

Example[a]	% Yield	Reference
	5-25[c]	11
 (camphidine) (cyclocamphidine)	67	12
	28-29	13
	15	14
	25	15
	~100	16
	69	16

a. All examples involved subsequent treatment with base to cause cyclization.
b. 11 Different substrates and products using various substituents R and R'.
c. 5 Different substrates and products using various substituents R.
d. No acid was added. Triethylamine was added to remove HCl as it formed.

abstraction.

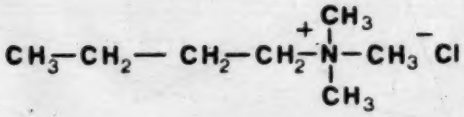
In the Hofmann-Lötfler-Freytag reaction the amine functionality exists primarily as the ammonium salt because of the highly acidic solvent.[57] The polar directing effect of this strongly electron-withdrawing group would be predicted to be large. Because of this effect the selectivity observed, from chlorine atom abstraction, may be such as to produce a product distribution similar to those which have been observed in the reactions proposed to occur by intramolecular abstraction.

Therefore, it was of interest to investigate further the propagation sequence of the intramolecular reaction, and attempt to obtain more concrete evidence as to the nature of the abstracting species.

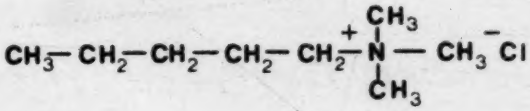
RESULTS

The chain propagation sequence for the intermolecular halogenation reactions, where product stability is not a consideration, appear to be reasonably well understood. On the basis of the selective production of pyrrolidine products (see Fig. 1), the mechanism of the intramolecular halogenations was suggested as proceeding by an intramolecular abstraction by a nitrogen-centered radical. It was not shown, however, that this mechanism could be distinguished from an intermolecular abstraction by a chlorine atom, or a nitrogen-centered radical which showed similar selectivities, and in light of the conclusions of Tanner and Mosher,[30] and Ingold and Spanswick[32] it appeared to be an important question to address.

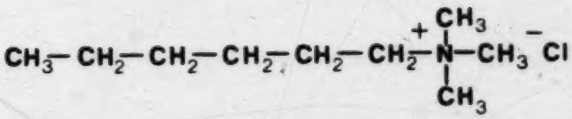
Since the amine substrates are considered to be almost completely protonated in the strong acid, the substrates n-butyltrimethylammonium chloride (I), n-pentyltrimethylammonium chloride (II), and n-hexyltrimethylammonium chloride (III) were chlorinated using molecular chlorine or N-chlorodimethylamine to investigate the polar effects exerted by the positive charge. Molecular chlorine was used as a source of all chlorine atoms in order to measure their selectivity, and



I

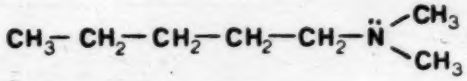


II



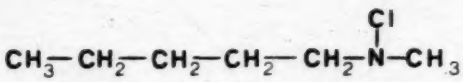
III

N-chlorodimethylamine was chosen as a source of a representative amminium radical, since it had been shown to give selectivities differing from chlorine atom.[32] A mixed acid, 15% CD_3CO_2D/85% H_2SO_4, was chosen as being representative of the solvents normally employed for the reaction. To measure the influence of the solvent upon the selectivity of the chlorine atom, a relatively non-polar solvent, hexachloroacetone, was also used with molecular chlorine. The use of the chloride salts with the N-chlorodimethylamine allowed the investigation of the suggested effect of chloride ion on the mechanism of N-chloroamine chlorinations.[30,32] To investigate the possible importance of unprotonated amine as the substrate, since it is always in equilibrium with the protonated amine, n-pentyldimethylamine (IV) was also

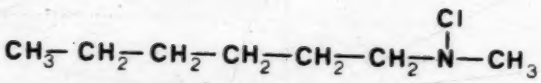


IV

chlorinated. Finally as models for the investigation of a potentially intramolecular abstraction process, the reactions of N-chloro-N-methyl-n-pentylamine (V) and N-chloro-N-methyl-n-hexylamine (VI) in 15% CD_3CO_2D/85% H_2SO_4 were studied.



V



VI

II.1 The Photochlorination of the Quaternary Ammonium Salts in Hexachloroacetone

Substrates I, II, and III were photochlorinated with molecular chlorine in hexachloroacetone at 30°C. The ratio of quaternary ammonium salt to molecular chlorine was made such that between 10 to 25 percent chlorination occurred. Lower percent chlorinations were very difficult to measure accurately, and higher percent

chlorinations ran the risk of being complicated by multiple chlorinations of individual substrate molecules. Oualitatively these chlorinations were quite slow, taking more than 6 hours to complete. The chlorination of 1-chlorobutane, for example, when run under similar conditions was complete in about 1 hour. The product yields were determined by nmr analysis.

The reactivities of the various hydrogens relative to the primary hydrogens in each of the quaternary salts are given in Table 1. The relative reactivities/H were calculated using equation 20 assuming the reactivity of the primary hydrogens to be unity.

$$R_x = \frac{3}{2} \cdot \frac{[\text{Product}]_x}{[\text{Product}]_1} \cdot R_1 \qquad (20)$$

R_x is the relative reactivity of the hydrogen in question, R_1 is the reactivity of the primary hydrogen (set to be unity), $[\text{Product}]_x$ is the concentration of product where the hydrogen in question has been exchanged for chlorine, $[\text{Product}]_1$ is the concentration of the product chlorinated at the primary position, and the Factor 3/2 corrects for the number of hydrogen atoms in question, relative to the number of primary hydrogen atoms.

Table I. Relative Reactivities/H in the Chlorinations of n-Butyltrimethylammonium Chloride, n-Pentyltrimethylammonium Chloride, and n-Hexyltrimethylammonium Chloride with Molecular Chlorine in Hexachloroacetone.[a,b]

Reaction #	$(CH_3)_3\overset{\oplus}{N}$ —	CH_2 —	CH_2 —	CH_2 —	CH_3		
1	0.0[c] (0)[e]	0.0 (0)	0.07±0.09[d] (1.5)	3.0±0.6 (66)	1.0 (33)		
	$(CH_3)_3\overset{\oplus}{N}$ —	CH_2 —	CH_2 —	CH_2 —	CH_2 —	CH_3	
2	0.0 (0)	0.0 (0)	0.0 (0)	1.8±0.6 (24)	4.1±1.1 (55)	1.0 (20)	
	$(CH_3)_3\overset{\oplus}{N}$ —	CH_2 —	CH_2 —	CH_2 —	CH_2 —	CH_2 —	CH_3
3	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	2.3±0.7 (28)	4.4±1.4 (54)	1.0 (18)

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. Reactions were irradiated with 2 x 100 watts incandescent lamps.
c. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.05.
d. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
e. (Percent yield), based on total products formed.

II.2 The Photochlorination of the Quaternary Ammonium Salts in 15% CD_3CO_2D/85% H_2SO_4

Substrates I, II, and III were photochlorinated with molecular chlorine in 15% CD_3CO_2D/85% H_2SO_4 at 30°C. The ratio of quaternary ammonium salt to molecular chlorine was made such that between 10 to 20 percent chlorination occurred. Qualitatively, these chlorinations required similar reaction times to those run using hexachloroacetone as the solvent. The product mixtures were analyzed by nmr.

The reactivities of the various hydrogens, relative to the primary hydrogens, in each of the quaternary salts are given in Table II.

A study of the ultraviolet absorption of molecular chlorine with changing sulfuric acid concentration was undertaken. The concentration of chlorine was held constant, while the concentration of sulfuric acid was changed from zero to concentrated H_2SO_4. No change in the ultraviolet absorption spectrum of chlorine was observed.

II.3 The Reaction of the Quaternary Ammonium Salts with N-Chlorodimethylamine in 15% CD_3CO_2D/85% H_2SO_4

To determine whether the chain carrying species in

Table II. Relative Reactivities/H in the Chlorinations of n-Butyltrimethylammonium Chloride, n-Pentyltrimethylammonium Chloride, and n-Hexyltrimethylammonium Chloride with Molecular Chlorine in 15% CD_3CO_2D/85% H_2SO_4.[a,b,c]

Reaction #	$(CH_3)_3\overset{\oplus}{N}$ —	CH_2 —	CH_2 —	CH_2 —	CH_3		
4	0.0[d] (0)[f]	0.0 (0)	0.0 (0)	2.1±0.4[e] (58)	1.0 (42)		
	$(CH_3)_3\overset{\oplus}{N}$ —	CH_2 —	CH_2 —	CH_2 —	CH_2 —	CH_3	
5	0.0 (0)	0.0 (0)	0.0 (0)	0.77±0.16 (21)	1.4±0.2 (38)	1.0 (41)	
	$(CH_3)_3\overset{\oplus}{N}$ —	CH_2 —	CH_2 —	CH_2 —	CH_2 —	CH_2 —	CH_3
6	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.73±0.08 (21)	1.2±0.2 (35)	1.0 (44)

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. The ratio was prepared volume/volume.
c. Reactions were irradiated with 2 x 100 watts incandescent lamps.
d. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.1.
e. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
f. (Percent yield), based on total products formed.

the Hofmann-Löffler-Freytag reaction is the chlorine atom or an amminium radical it is necessary to know what the reactivity of the chlorine atom is for the chosen substrates, and then to compare this reactivity with that shown by a representative N-chloroamine. N-Chlorodimethylamine was chosen as a typical example for comparison, since it is easily prepared in pure form[32] and should be relatively unreactive with itself.

The N-chlorodimethylamine was prepared following the procedure of Ingold,[32] since he had shown that material prepared in this manner gave reactivities not attributable to a chlorine atom chain. The N-chloroamine was stored in 15% CD_3CO_2D/85% H_2SO_4 at -78°C until it was used to chlorinate the quaternary ammonium salts.

Substrates I, II, and III were photochlorinated with N-chlorodimethylamine at 30°C in 15% CD_3CO_2D/85% H_2SO_4. The reactions were qualitatively quite slow, taking up to 120 hours for complete reaction of the N-chloroamine. Since the mixtures were irradiated through pyrex ampoules with incandescent light, the reactions may have been slow because of poor photolysis of the N-chloroamine. The reaction with the n-hexyl salt, III, however, was complete in 24 hours, as was its reaction with molecular chlorine. The product mixtures were analyzed by nmr.

The ratio of N-chlorodimethylamine to quaternary

ammonium salt was made such that between 10 and 18 percent chlorination occurred. The reactivities of the various hydrogens, relative to the primary hydrogens, in each of the quaternary salts are given in Table III.

II.4 The Chlorinations of n-Pentyldimethylamine in 15% CD_3CO_2D/85% H_2SO_4

The chlorinations of amine IV in 15% CD_3CO_2D/85% H_2SO_4 with molecular chlorine, and with N-chlorodimethylamine were carried out in order to investigate the reactivity of a compound which was positively charged when protonated. If chlorination of the unprotonated species is sufficiently favored over that of the protonated species, then even though the concentration of unprotonated amine is very much lower than that of the protonated amine, it is possible that the relative reactivities observed will represent those of the unprotonated amine. Thus, having the relative reactivites of quaternary salt II to compare with, the relative reactivities of amine IV can provide some insights into the importance of protonation of the substrate.

Amine IV was chlorinated in 15% CD_3CO_2D/85% H_2SO_4 with molecular chlorine and with N-chlorodimethylamine in the same manner as previously described for the

Table III. Relative Reactivities/H in the Chlorinations of n-Butyltrimethylammonium Chloride, n-Pentyltrimethylammonium Chloride, and n-Hexyltrimethylammonium Chloride with N-Chlorodimethylamine in 15% CD_3CO_2D/85% H_2SO_4.[a,b,c]

Reaction #	$(CH_3)_3\overset{\oplus}{N}$ —— CH_2 —— CH_2 —— CH_2 —— CH_3				
7	0.0[d] (0)[f]	0.0 (0)	0.31±0.03[e] (4.8)	4.6±0.3 (72)	1.0 (23)

	$(CH_3)_3\overset{\oplus}{N}$ —— CH_2 —— CH_2 —— CH_2 —— CH_2 —— CH_3					
8	0.0 (0)	0.0 (0)	0.0 (0)	0.54±0.17 (3.2)	15.1±1.5 (88)	1.0 (8.8)

	$(CH_3)_3\overset{\oplus}{N}$ —— CH_2 —— CH_2 —— CH_2 —— CH_2 —— CH_2 —— CH_3						
9	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	2.3±0.1 (11)	18.0±1.4 (83)	1.0 (6.9)

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. The ratio was prepared volume/volume.
c. Reactions were irradiated with 2 x 100 watts incandescent lamps.
d. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.1.
e. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
f. (Percent yield), based on total products formed.

quaternary ammonium salts. The results obtained are given in Table IV.

II.5 The Photochlorinations of N-Chloromethyl-n-pentylamine and N-Chloromethyl-n-hexylamine in 15% CD_3CO_2D/85% H_2SO_4

The Hofmann-Loffler-Freytag reaction has been proposed to proceed by the intramolecular hydrogen abstraction of an amminium radical, in cases where the nitrogen atom can abstract in a 5, 6 or 7 membered cyclic transition state.[3] Since a method was now available for analysis of the products without the complications arising from treatment with base, these reactions were reinvestigated.

N-chloroamines V and VI were prepared from the corresponding amines by the procedure of Coleman,[2] and photolyzed at 30°C in 15% CD_3CO_2D/85% H_2SO_4 with incandescent light. The reactions were qualitatively faster than the chlorinations of the quaternary salts with N-chlorodimethylamine, taking less than 24 hours to complete. The product mixtures obtained were analyzed by nmr, and the results obtained are given in Table V.

Table IV. Relative Reactivities/H in the Chlorination of n-Pentyldimethylamine with Molecular Chlorine or N-Chlorodimethylamine in 15% CD_3CO_2D/85% H_2SO_4.[a,b,c]

Reaction #	Chlorinating Reagent	$(CH_3)_2N-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_3$
10	Cl_2	0.0[d] (0)[f]	0.0 (0)	0.0 (0)	1.3±0.2[e] (21)	3.3±0.7 (54)	1.0 (25)
11	$(CH_3)_2NCl$	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0))	12.7±0.9 (89)	1.0 (11)

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. The ratio was prepared volume/volume.
c. Reactions were irradiated with 2 x 100 watts incandescent lamps.
d. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.1.
e. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
f. (Percent yield), based on total products formed.

Table V. Relative Reactivities/H in the Self Chlorinations of N-Chloro-n-pentylmethylamine and N-Chloro-n-hexylmethylamine in 15% CD_3CO_2D/85% H_2SO_4.[a,b,c]

Reaction #	$CH_3-\overset{Cl}{\underset{|}{N}}-CH_2-CH_2-CH_2-CH_2-CH_3$					
12	0.0[d] (0)[f]	0.0 (0)	0.0 (0)	0.33±0.10[e] (0.25)	129±11 (99)	1.0 (1.1)

Reaction #	$CH_3-\overset{Cl}{\underset{|}{N}}-CH_2-CH_2-CH_2-CH_2-CH_2-CH_3$						
13	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	115±5 (81)	25.5±0.7 (18)	1.0 (1.4)

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C.
b. The ratio was prepared volume/volume.
c. Reactions were irradiated with 2 x 100 watts incandescent lamps.
d. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 0.1.
e. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.
f. (Percent yield), based on total products formed.

II.6 Control Experiments

As a precaution to ensure that the N-chlorodimethylamine prepared here was of the same purity as that prepared by Ingold,[32] the chlorination of 1-chlorobutane in 15% CH_3CO_2H/85% H_2SO_4 with N-chlorodimethylamine was carried out. The reaction mixtures were diluted with H_2O and extracted into CCl_4. Freon 112 was used as an internal standard and the product yields were determined by Glpc analysis. The results obtained are given in Table VI.

The relative reactivities given in Tables I through V contain large errors. These errors appear to be due to the method of analysis, since in hexachloroacetone, where the amount of product handling is greatest, the error is largest, the error being less in the 15% CD_3CO_2D/85% H_2SO_4, and least in the analyses done by Glpc. Therefore control experiments were run to determine the reliability of the nmr measurements.

A weighed mixture of quaternary salt II, 5-chloro-n-pentyltrimethylammonium chloride, 4-chloro-n-pentyltrimethylammonium chloride, and 3-chloro-n-pentyltrimethylammonium chloride was dissolved in hexachloroacetone, and the product mixture was subjected to the same analytical procedure as was used for the reaction mixtures. The results are given in Table VII.

A similar mixture was prepared and dissolved in 15%

Table VI. Relative Reactivities/H in the Chlorination of 1-Chlorobutane with N-Chlorodimethylamine in 15% CH_3CO_2H/85% H_2SO_4.[a]

Reaction #	Reagent	$Cl-CH_2$ ——	CH_2 ——	CH_2 ——	CH_3	Reference
	$(CH_3)_2NCl,h\nu$	0.56 (4.7)[c]	1.8 (14.8)	8.1 (67.9)	1.0 (12.6)	32[b]
	$(CH_3)_2NCl$,AIBN	1.2 (4.8)	2.7 (10.6)	20.4 (78.8)	1.0 (5.8)	32[b]
14	$(CH_3)_2NCl,h\nu$	0.75±0.07[d] (4.1)	1.4±0.1 (7.7)	14.6±0.5 (80)	1.0 (8.2)	This Work
	$Cl_2,h\nu$	0.38 (5.4)	1.5 (20.9)	3.6 (52.0)	1.0 (21.6)	30

a. Reactivity per hydrogen atom relative to the primary hydrogen at 30°C. Irradiation with 2 x 100 watts incandescent lamps.
b. Done in $4M H_2SO_4/CH_3CO_2H$.
c. (Percent yield), based on total products formed.
d. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.

CD_3CO_2D/85% H_2SO_4, and analyzed in the same manner as described for the reaction mixtures. The results are given in Table VIII.

In both of the control experiments the errors obtained ranged up to 13%. Thus the major portion of the errors shown for the results given in Tables I through V are likely to arise from the method of analysis.

The relative reactivities in hexachloroacetone (Table I) appear to be different from those obtained in 15% CD_3CO_2D/85% H_2SO_4 (Table II). Because of the polarity of the acid solvent, it is possible that the relative reactivities in this solvent reflect selective decomposition of some of the products. If products are unstable in this solvent, the change in selectivity when chlorinating in 15% CD_3CO_2D/85% H_2SO_4 may be entirely due to selective destruction of products.

To test the stability of the products in 15% CD_3CO_2D/85% H_2SO_4, quaternary salt II was chlorinated in hexachloroacetone at 30°C with molecular chlorine. The products were quantitatively determined, and the solvent removed by distillation under reduced pressure. The products were redissolved in an appropriate amount of 15% CD_3CO_2D/85% H_2SO_4 and irradiated at 30°C for the same amount of time as the photochlorinations. The products were reanalyzed; as can be seen in Table IX the product ratios, within experimental error, had not changed.

Table VII. Reliability of NMR Measurements in hexachloroacetone.[a]

Compound	Mole % Calculated	Mole % Found	Error, %
II	75.61	75.44	1.1
$Cl\text{-}(CH_2)_5\overset{\oplus}{N}(CH_3)_3\overset{\ominus}{Cl}$	4.44	4.97	11.3
$CH_3CHCl(CH_2)_3\overset{\oplus}{N}(CH_3)_3\overset{\ominus}{Cl}$	14.21	12.39	13.7
$CH_3CH_2CHCl(CH_2)_2\overset{\oplus}{N}(CH_3)_3\overset{\ominus}{Cl}$	5.74	6.20	7.7

a. A weighed mixture of the compounds was dissolved in hexachloroacetone and treated in the same manner as reactions run in this solvent.

Table VIII. Reliability of NMR Measurements in 15% CD_3CO_2D/85% H_2SO_4.[a]

Compound	Mole % Calculated	Mole % Found	Error, %
II	33.64	34.43	2.3
$Cl\text{-}(CH_2)_5\overset{\oplus}{N}(CH_3)_3\overset{\ominus}{Cl}$	25.50	26.58	4.2
$CH_3CHCl(CH_2)_3\overset{\oplus}{N}(CH_3)_3\overset{\ominus}{Cl}$	16.16	17.30	6.8
$CH_3CH_2CHCl(CH_2)_2\overset{\oplus}{N}(CH_3)_3\overset{\ominus}{Cl}$	24.70	21.69	13.0

a. A weighed mixture of the compounds was dissolved in 15% CD_3CO_2D/85% H_2SO_4 and treated in the same manner as reactions run in this solvent.

Table IX. Stability of Products in 15% CD_3CO_2D/85% H_2SO_4.[a]

Reaction #	Solvent	$(CH_3)_3\overset{\oplus}{N}$ —	CH_2 —	CH_2 —	CH_2 —	CH_2 —	CH_3
15	$Cl_3CCOCCl_3$	0.0[b,c]	0.0	0.0	19.8±5.0[d]	58.6±3.2	21.6±4.7
15[e]	15% CD_3CO_2D/ 85% H_2SO_4	0.0[f]	0.0	0.0	22.7±1.3	58.7±2.4	18.6±3.7

a. Products from the photochlorination at 30°C with molecular chlorine; irradiated with 2 x 100 watts incandescent lamps.

b. Percent of total products formed.

c. Relative reactivities of 0.0 indicate that no product was detected; the limit of detection being 1.3%.

d. The errors given are the average deviation from the mean. All values represent the results of at least three independent experiments.

e. The solvent, hexachloroacetone, was removed by vacuum distillation and the product residue was dissolved in an appropriate amount of 15% CD_3CO_2D/85% H_2SO_4 and irradiated at 30°C for 24 hours.

f. The limit of detection was 2.5%

DISCUSSION

Polar effects in hydrogen abstraction reactions have been recognized in many free-radical substitutions.[58,59] Walling and Russell[60-62] have presented convincing arguments for the importance of polar contributions to the transition state leading to hydrogen abstraction. Three major canonical forms of the transition state can be considered. The first (19) would predominate when the abstracting radical X· has an electronegativity, or polarizability similar to that of carbon, such that no charge separation occurs. The second (18) would be expected to be heavily weighted when the abstracting radical is less electronegative than carbon, such that X supports a partial positive charge, and the carbon atom a partial negative charge. The third (20) would be expected to be heavily weighted when the abstracting radical is more electronegative than carbon, such that X supports a partial negative charge, and the carbon a

18 19 20

partial positive charge. The importance of the polar structures is also dependent upon the extent to which the carbon-hydrogen bond is broken in the transition state. The more the bond is stretched (i.e. the more stable X· is) the greater the extent of charge separation. Hence more stable, or less reactive, radicals should show larger polar sensitivities than more reactive radicals of similar electronegativity or polarizability.

Hammett ρ values for abstraction of benzylic hydrogens from substituted toluenes, using σ or σ^+ substituent constants, have been used as indicators of the sensitivity to polar effects for various abstracting species.[58,59] The magnitude of ρ is representative of the reactivity of the abstracting species and the size of the polar effect. The sign of ρ indicates the electron demand for the abstracting radical, a negative value of ρ indicating that electron donors increase the reaction rate. Consequently for the chlorine atom, with a ρ of -0.66,[29] canonical form 20 would be expected to be dominant.

For a 1-substituted butane with an electron withdrawing group, two opposing trends combine to form the reactivities commonly observed. Bond dissociation energies yield selectivities where the α-hydrogens are most reactive because of resonance stabilization and the

δ-hydrogens are least reactive since they are the only primary hydrogens. The β-secondary hydrogens are assumed to be more reactive than the γ-hydrogens, due to hyperconjugation differences and other interactions, although bond dissociation energy differences are not known. The polar directing effect of the electron withdrawing group works in opposition to the selectivities. The charge separation present in the transition state causes abstraction to be more favorable at carbons further removed from the electron withdrawing group.

III.1 Chlorinations in Hexachloroacetone

Chlorination of 2,3-dimethylbutane with molecular chlorine in this solvent showed a tertiary to primary selectivity/H (4.0:1) very similar to that obtained when the chlorination was carried out in CCl_4 (3.5:1); a variety of selectivities in CCl_4 has been reported previously, 5.1:1 at 27°C,[63] 3.5:1 at 55°C,[64] and 4.2:1 at 25°C[65] (no solvent). Therefore, a comparison of the relative reactivities to molecular chlorine of several 1-substituted butanes, pentanes and hexanes in CCl_4 with the reactivities observed for the quaternary salts is instructive. Two major observations from comparison of

Tables I and X are noteworthy. At carbons further than two removed from the substitution, the relative reactivities obtained with the quaternary ammonium salts compare well with those listed in Table X. The relative reactivities rapidly drop to zero, however, in the quaternary ammonium salts as the nitrogen center is approached. Steric blocking by the trimethylammonium group is most likely an important factor in the reactivities of the α- and β-hydrogens. The influence of a polar effect by the positively charged nitrogen, however, must also be an important factor in determining the relative reactivities of the sites, since a marked decrease in the reactivity was observed for the γ-hydrogens in quaternary salt III. Under similar conditions the chlorination of 1-chlorobutane was complete in less than 1 hour, however active chlorine could be detected even after 6 hours when the quaternary salts were chlorinated. This implies deactivation of the salts toward hydrogen abstraction causing the termination step, 21, to be relatively more important.

$$2\,Cl\cdot \longrightarrow Cl_2 \qquad (21)$$

Table X. Relative Hydrogen Reactivities in Various Substituted Alkanes to Molecular Chlorine.

X ———	CH_2 ——	CH_2 ——	CH_2 ——	CH_3	Temp, (°C)[a]	Solvent[b]	Ref.
Cl-	0.30	1.20	2.23	1.0	20	CCl_4	66
Br-	0.21	1.93	3.50	1.0	60	Neat	67
F-	0.45	0.89	1.90	1.0	20	Freon 113	66
Cl_2-	0.23	0.42	1.81	1.0	80	Neat	68
Cl-C(=O)-	0.19	0.80	2.10	1.0	20	CCl_4	66
F-C(=O)-	0.08	1.57	4.20	1.0	65-70	gas	69
CH_3C(=O)-O-	0.07	1.20	2.51	1.0	40	CH_3CN	70
Cl_3CC(=O)-O-	0.0	0.15	1.10	1.0	80	---	68
CF_3C(=O)-O-	0.09	0.76	2.09	1.0	53	CCl_4	70
Cl-S(=O)(=O)-	0.0	0.10	2.61	1.0	80	---	68

continued.....

Table X (continued):

CF_3-	0.03	1.11	4.55	1.0		20	gas	66
CH_3-O-C(=O)-	0.43	2.42	3.56	1.0		55-60	gas	69
C_6H_5-	6.30	2.85	4.20	1.0		40	CCl_4	71
CH_3O-	3.50	0.70	4.30	1.0		50	gas	71
N≡C-	0.23	1.69	3.85	1.0		110	gas	72

X——	CH_2 ——	CH_2 ——	CH_2 ——	CH_2 ——	CH_3	Temp. (°C)	Solvent	Ref.
Cl-C(=O)-	0.15	0.58	1.56	2.00	1.0	20	CCl_4	66
F-C(=O)-	0.16	1.46	4.05	4.52	1.0	50	gas	70
Cl-	0.80	1.99	3.74	5.50	1.0	78	gas	73
F-	0.79	1.34	3.07	4.41	1.0	78	gas	73

continued.....

Table X (continued):

X—	CH_2	CH_2	CH_2	CH_2	CH_2	CH_3	Temp. (°C)	Solvent	Ref.
F-C(=O)-	0.21	1.76	4.12	4.11	4.46	1.0	60	gas	70
Cl-C(=O)-	0.04	0.41	0.89	1.12	1.39	1.0	52	CH_3CN	70

a. Temperatures differing greatly from 30°C (conditions of this study) may be poor comparisons.
b. Tedder[74] has shown the relative reactivities of various substituted hydrocarbons to be dependent on the solvent in which they were chlorinated.

Ultraviolet irradiation of hexachloroacetone can be used to produce trichloromethyl radicals. Reaction mixtures prepared without addition of molecular chlorine, however, showed the quaternary salts to be stable to the reaction conditions, and no chloroform was observed to have formed.

III.2 Chlorinations with Molecular Chlorine in 15% CD_3CO_2D/85% H_2SO_4

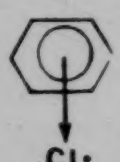
The Hofmann-Löffler-Freytag reaction is normally carried out in acidic media and initiated either thermally or by light. If the solvent's only function is to protonate the amine, forming the ammonium salt, then the chlorination of the quaternary salts with molecular chlorine should give similar relative reactivities in the acidic solvent as in the hexachloroacetone. If, however the solvent is more intimately involved in affecting transition state differences, the relative reactivities obtained should show a dependence on the solvent used.

A comparison of the relative reactivities, of the different sites of the ammonium salts, in hexachloroacetone (Table I) with those carried out in 15% CD_3CO_2D/85% H_2SO_4 (Table II) shows a significant difference in product distribution. The most obvious

difference is an apparent increase in the relative reactivities of the hydrogens located on the terminal carbons. For salts II and III the products from chlorination at the terminal carbon are the major products observed.

The overall result is an apparent increase in the polar effect exerted by the quaternary nitrogen group. Since the results in Table IX show that the products formed are stable to the reaction conditions, selective product destruction by the solvent, 15% CD_3CO_2D/85% H_2SO_4, is eliminated as an explanation for the change in the observed relative reactivities.

Solvent effects in free radical reactions are rare and usually small. If large solvent effects are observed they have generally been shown to be due to complexed radicals; examples are chlorine atoms in benzene and in carbon disulfide.[64,65,75] The abstracting species 21 and 22 respectively have been proposed to be the abstracting radicals in these solvents.



(π-complex)

21

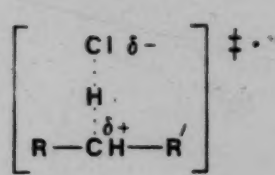
$CS_2Cl\cdot$

22

The ultraviolet study of chlorine absorption vs

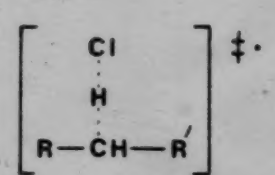
concentration of sulfuric acid did not produce any evidence supporting the formation of a complexed chlorine atom. This study, however, would not detect a radical of low concentration and small molar extinction coefficient. Further support for the chlorine atom being uncomplexed in the acidic solvent comes from the work of Tanner and Mosher.[30] They found the product distribution for the chlorination of 1-chlorobutane with molecular chlorine to be essentially identical in carbon tetrachloride and in 15% CH_3CO_2H/85% H_2SO_4.

An explanation of the observed change in relative reactivities involves the polar natures of the two solvents concerned. In the less polar hexachloroacetone the polar contribution to the transition state, 23,



23

should be poorly stabilized by the solvent molecules and hence its importance may be small relative to the nonpolar contribution, 24. In the more polar 15%



24

CD_3CO_2D/85% H_2SO_4 the polar contribution to the transition state, 23, should be better stabilized, and its importance should be greater than in the hexachloroacetone. The observed greater polar directing effect in the acid solvent would therefore be due to the greater importance of the polar contribution to the transition state, 23. This is in line with the observation that chlorination of 2,3-dimethylbutane with molecular chlorine in 15% CH_3CO_2H/85% H_2SO_4 indicated a tertiary to primary selectivity/H of 3.3:1 very similar to those obtained in the non-acid solvents (4.0:1 in hexachloroacetone, 3.5:1 in CCl_4).

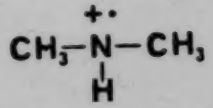
III.3 Chlorinations with N-Chlorodimethylamine

Comparison of the observed relative reactivities obtained with molecular chlorine in 15% CD_3CO_2D/85% H_2SO_4 (Table II), and those obtained from chlorinations carried out using N-chlorodimethylamine in the same solvent (Table III) shows a large difference. Two major changes are apparent. With N-chlorodimethylamine the polar directing effect is larger (the ω-2 chlorination has decreased relative to the ω-1 plus ω positions) than observed with molecular chlorine, and the primary to secondary selectivity (for the terminal and penultimate

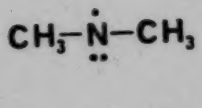
carbons) is greater than observed with molecular chlorine.

The difference in polar directing effects for reaction with molecular chlorine and with N-chlorodimethylamine is measurable, but reasonably small. The selectivity difference is the more obvious change and indicates a less energetic abstracting species is involved. The selectivity observed is very high and dominates the relative reactivities. In the short chain salt, I, the effect appears to be diminished due to the proximity of the polar group (reaction 7, Table III). In the longer chain salts, II and III, as the polar group is further removed the selectivity of the abstracting species becomes more obvious.

The large difference in relative reactivities obtained with N-chlorodimethylamine versus those obtained with molecular chlorine indicate that two different abstracting species are involved. The only other reasonable candidates in the reactions with N-chlorodimethylamine are the aminium radical, 25, and the amino radical, 26.



25



26

The initiation sequence could conceivably involve the N-chloroamine, protonated N-chloroamine, or fortuitous small quantities of molecular chlorine present. The protonated N-chloroamine is reported to have no UV absorptions above 225 nm,[76] and therefore, because of the light source and the Pyrex ampoules used in the reactions, the protonated N-chloroamine is not likely to be the source of initiating radicals. The unprotonated N-chloroamine has an absorption at 263 nm, however based on the reported K_b[63] of 2.9×10^{-14} (in H_2O) the calculated concentration in sulfuric acid ($\sim 10^{-9}$ M), is too low to be a significant source of initiation. Initiation is most likely a combination of thermal initiation (even though slow at 30°C) and initiation by fortuitous trace amounts of molecular chlorine in the solution.

For the propagation sequence chlorine atoms may be in competition, but the relative reactivities indicate a major contribution from radicals 25 or 26. Only if abstraction by the amino radical, 26, is highly favored over the amminium radical, 25, can the amino radical be the important abstracting species. If the previous condition is not true, however, the much greater concentration of amminium radical, 25, would cause it to be the dominant abstracting species.

Tedder[74] has argued in favor of the amino radical,

26, as the abstracting species based on consideration of the repulsion between the new radical, R·, and new molecule, X-H, and the repulsion between the incoming radical, X·, and the substrate molecule, R-H (see equation 22). These considerations were said to favor

$$X\cdot + R\text{-}H \longrightarrow X\text{-}H + R\cdot \qquad (22)$$

the amino radical as the abstracting species since repulsion between the amminium radical and the ammonium substrate would tend to make their approach unfavorable, but the amino radical and the ammonium substrate would attract each other. The high selectivity of abstracting observed for the amminium radical, relative to that of the chlorine atom, appears to be in conflict with the low isotope effect ($k_H/k_D = 1.2$) observed by Green[45] for the reaction of N-chloroamines initiated by Fe II (see equation 18). This high selectivity, however, is in better agreement with the result of Corey[3] ($k_H/k_D = 3.48$) for the reaction of N-chloroamines initiated thermally (see equation 19), and may indicate the incursion of a chlorine atom chain with the Fe II reagent as was suggested by Ingold.[32]

Since sulfuric acid catalyzes the reactions, protonated species must participate in acceleration of the initiation or propagation sequences, inhibition of the

termination steps, or all three. Termination could be inhibited by the acid, since reaction of two amminium radicals (equation 23) would be highly unfavorable due

$$2R_2\overset{+\cdot}{N}-H \longrightarrow R_2\overset{+}{N}(H)-\overset{+}{N}(H)R_2 \qquad (23)$$

to coulombic repulsion of the positive charges, whereas, in the absence of sulfuric acid, the same termination step between two amino radicals would be favored, if this is the important reaction. The initiation sequence might be accelerated if thermal decomposition of the protonated N-chloroamine is faster than that of the N-chloroamine. The chlorine atom transfer step (equation 24) between the protonated N-chloroamine and the alkyl radical has been

$$R\text{-}CH_2\cdot + R_2'\overset{+}{N}HCl \longrightarrow RCH_2Cl + R_2\overset{+\cdot}{N}H \qquad (24)$$

suggested[74] to be enhanced due to coulombic attraction between the radical and the positively charged N-chloroamine. This, however, is probably not as important as the effects on initiation and termination.

Ingold[32] suggested that N-chlorodimethylamine, which gave chlorine atom selectivities was due to insufficiently pure N-chloroamine (the impurity, chloride ion, reacting with the N-chloroamine to yield molecular chlorine). The N-chloroamine when prepared by his procedure was said

to be sufficiently pure to give relative reactivities not attributable to chlorine atoms, when the reaction was initiated with AIBN. If the reaction, however, was initiated with light the relative reactivities obtained were lower (approaching values obtained with molecular chlorine), and thus represented a reaction contaminated by a chlorine atom chain. Table VI compares the results obtained from the photochlorination of 1-chlorobutane with N-chlorodimethylamine, prepared by the procedure of Ingold, those previously obtained by Ingold with light and AIBN, and the results from chlorination with molecular chlorine obtained by Tanner.[30] The results obtained in this study agree most closely with Ingold's results with AIBN initiation, suggesting that the reagent used in this study is of comparable or better purity than that previously reported.[32] It is also important to note that although chloride ion was added to these reactions, as the counter ion of the quaternary salts, it did not cause the reaction to occur by a chlorine atom chain. Either the previous suggestions that chloride ion causes the change are not correct, or the chloride ion, in these substrates, is intimately associated with the ammonium salts, even in the highly polar acidic solvent.

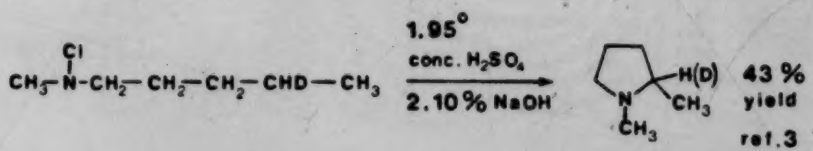
III.4 Chlorinations of n-Pentyldimethylamine (IV)

Table IV gives the results of the photochlorination of amine IV using molecular chlorine or N-chlorodimethylamine in 15% CD_3CO_2D/85% H_2SO_4. Comparison of reaction 10 with reaction 5 (Table II) and reaction 11 with reaction 8 (Table III) indicates very similar relative reactivities were obtained with ammonium salt II and amine IV. Amine IV may actually exhibit a greater polar directing effect than the salt, II. This result suggests that abstraction from the unprotonated amine is not important and that the amine must exist almost exclusively as the ammonium salt. The difference observed between reaction 10 (Table IV) and reaction 5 (Table II) (an apparent increase in δ-chlorinated product) may be due to the intramolecular reaction of some N-chloro-n-pentyldimethylamine, formed from reaction with the chlorine, since this reaction has been documented previously.[35]

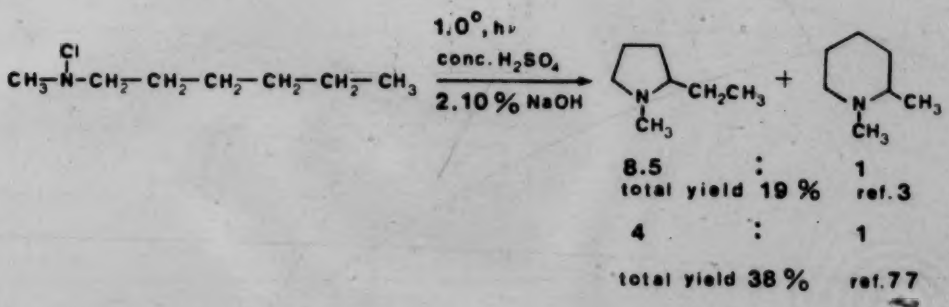
III.5 Intramolecular Abstraction vs Intermolecular Abstraction

Wawzonek and Culbertson[77] and Corey and Hertler[3] investigated the products from cyclization of N-chloro-

amine VI. Corey and Hertler also investigated the products from the 4-deuterio-analog of N-chloroamine V. The results they obtained are shown in equations 25 and 26. The yields obtained in these reactions were poor, and the product distributions differ considerably. Based on these results both groups concluded that the hydrogen transfer occurred through an intramolecular abstraction (equation 27) rather than an intermolecular abstraction (equation 28).

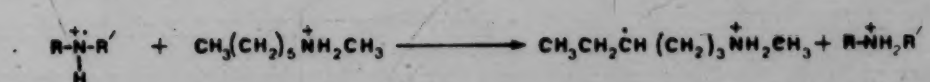


(25)



(26)

(27)



(28)

Since the isolated yields reported are low, they are obviously not accurate representations of the hydrogen abstraction selectivities. Both reports noted that residual unidentified material remained after the cyclized products were isolated. During the treatment with sodium hydroxide those chlorinated amines which are not sterically prevented from doing so, cyclize. Chlorinated amines which do not readily cyclize, and some of those which do, are never isolated because they polymerize to high molecular weight products. Elimination of hydrogen chloride to yield olefinic products, through treatment with sodium hydroxide, also decreases the yield of cyclized product obtained.

For the reactions of N-chlorodimethylamine with the quaternary salts only three abstracting species were considered: the chlorine atom, the amino radical, or the amminium radical. For reactions of N-chloroamines V and VI not only the abstracting species need be considered, but also the nature of the substrate. The possible mechanisms can be divided into two groups depending upon whether the hydrogen abstraction is intramolecular or intermolecular.

Based on the arguments presented for the concentration of amines in the acid solvent, the N-chloroamine and the amine can be eliminated as substrates, and the amino radical can most likely be eliminated as an abstracting species for an intermolecular abstraction. The protonated N-chloroamine would most likely serve as substrate in the initial stages of the reaction, while the protonated amine (formed from reaction with HCl) would compete at the end of the reaction. The relative reactivities of the quaternary salts presented in Table V are very different from those obtained from the chlorination, with molecular chlorine (reactions 5 and 6, Table II). This observation eliminates the chlorine atom as the abstracting species.

Comparison of reaction 12 (Table V) with reaction 11 (Table IV) or reaction 8 (Table III), assuming the small differences are due to the different N-chloroamines used, would suggest that an intermolecular abstraction by the amminium radical could be responsible for the relatively specific reactivities observed in the supposedly intramolecular reactions. However, comparison of reaction 13 (Table V) with reaction 9 (Table III), is strong evidence for intramolecular hydrogen abstraction, since the 4-chloroproduct (the product from a six-membered internal abstraction transition state) is still the major product

for N-chloroamine VI. Since it is unlikely that N-chloroamines V and VI should react by different mechanisms, it can be concluded that both substrates react by an intramolecular hydrogen abstraction.

Unless the intramolecular abstraction by the amino radical is highly favored, the amminium radical must be the intermediate because of its much greater concentration. Abstraction by the amminium radical would be expected to be slower, due to the highly polar transition state, however intramolecular abstraction would still be expected to occur rapidly due to its favorable activation entropy.

The percentage yields of the products are given in Table V. Comparison of these values with those reported previously (equations 25 and 26) show that the yields obtained in this nmr study are much greater than the isolated yields reported. These numbers can be considered to represent the true abstraction selectivities obtained. The results from N-chloroamine V indicate a yield of 99% of the N-methylpyrrolidine, if cyclization were 100% efficient. The results from N-chloroamine VI indicate a yield of 81% for 2-ethyl-1-methylpyrrolidine and 18% of 1,2-dimethylpiperidine if cyclization were 100% efficient. All of the reported yields (equations 25 and 26) are lower, and the ratio of the pyrrolidine to piperidine

obtained from N-chloroamine VI reported by Corey,[3] is much larger than those suggested from the values listed in Table V. This difference in results is most likely due to the isolation steps, during which cyclization of the chlorinated amine occurs. Wawzonek[77] obtained a higher yield of isolated products than Corey,[3] and also obtained a similar ratio of the pyrrolidine to the piperidine as is suggested by Table V. This supports the suggestion that the discrepancies are due to inefficient isolation of products.

In summary, high selectivity of product formation, based on incomplete product yields, has been used as evidence for an intramolecular abstraction mechanism. On the basis of the complete product studies in this work, the intramolecular abstraction mechanism still best explains the results obtained.

In contrast with the conclusions of Ingold and Tanner, on the mechanism of the intermolecular analog, the intramolecular reactions do not appear to be sensitive to the method used to prepare the reagent.

The high selectivities previously observed are most likely the result of incomplete cyclization during the treatment with strong base, as are reflected in the low yields obtained.

EXPERIMENTAL

IV.1 Materials

Hexachloroacetone (Eastman) was distilled at 28-32°C at 0.3 mm Hg pressure through an 8" Vigreux column. 400 MHz ^1H nuclear magnetic resonance spectrometry showed it to contain no observable protons under the conditions of analysis.

Carbon tetrachloride (Fisher Scientific Co.) was distilled over P_2O_5 before use. Glpc analysis showed it to be >99.9% pure.

Sulfuric Acid (Fisher Scientific Co.) was used without further purification.

Perdeuterioacetic acid (99.5% D Fisher Scientific Co.) was used without further purification.

Perdeuterioacetonitrile (99% D Merck Sharp and Dohme Canada Limited) was used without further purification.

Chlorine (Matheson) was bubbled through concentrated sulfuric acid, glass wool and sodium hydroxide pellets.

2,3-Dimethylbutane (Phillips Petroleum Company, Research Grade >99.88%) was used without further purification.

1-Chlorobutane (Matheson Coleman and Bell) was distilled through an 18" Vigreux column. Glpc analysis showed it to be >99.9% pure.

IV.2 Instrumentation

Nmr spectra,400 MHz ^1H, were obtained using a Bruker WH-400 nmr spectrometer; 90 MHz ^1H nmr spectra were obtained with a Perkin-Elmer R32 nmr spectrometer, and 60 MHz ^1H nmr spectra were obtained using a Varian A-56/60A nmr spectrometer. Glpc analyses were done using a Carlo Erba Fractovap Mod. GV gas chromatograph equipped with a flame ionization detector. The product mixtures were quantitatively measured using a calibration mixture of the authentic materials plus the standard used. Mass spectra were run with an AEI model MS12 mass spectrometer. Ultraviolet spectra were obtained with a Unicam SP1700 ultraviolet spectrophotometer.

IV.3 Compounds

Quaternary Ammonium Salts

The ammonium salts were prepared from the appropriate 1-chloroalkane and trimethylamine according to the procedure of Smith and Frank.[78]

n-Butyltrimethylammonium chloride was prepared from 1-chlorobutane and trimethylamine at 60°C in methanol. The solvent was removed by rotary evaporation and the resulting white solid was washed several times with diethyl ether, filtered and dried under vacuum at 60°C: mp 225-230°C (dec.), (lit.[79] mp 223.7-224°C); 400 MHz ^1H nmr data (CD_3CN) δ 1.00 (t, J = 7 Hz, 3H), 1.43 (m, 2H), 1.81 (m, 2H), 3.15 (s, 9H), 3.36 (m, 2H).

n-Pentyltrimethylammonium chloride was prepared from 1-chloropentane and trimethylamine[80] at 60°C in methanol. The solvent was removed by rotary evaporation and the resulting white solid was washed several times with diethyl ether, filtered and dried under vacuum at 60°C: mp 197-199°C; 400 MHz ^1H nmr data (CD_3CN) δ 0.95 (t, J = 7 Hz, 3H), 1.40 (m, 4H), 1.83 (m, 2H), 3.15 (s, 9H), 3.35 (m, 2H).

n-Hexyltrimethylammonium chloride was prepared from 1-chlorohexane and trimethylamine[81] at 60°C in methanol. The solvent was removed by rotary evaporation and the resulting white solid was washed several times with diethyl ether, filtered and dried under vacuum at 60°C: mp 197-197.5°C; 400 MHz ^1H nmr data (CD_3CN) δ 0.995 (t, J = 5 Hz, 3H), 1.46 (m, 6H), 1.85 (m, 2H), 3.15 (s, 9H), 3.30 (m, 2H).

4-Chloro-n-butyltrimethylammonium chloride was prepared from 1,4-dichlorobutane and trimethylamine at 60°C in methanol. The solvent was removed by rotary evaporation and the resulting white solid was washed several times with diethyl ether, filtered and dried under vacuum: mp 148-151°C; 400 MHz ^{1}H nmr data δ 1.90 (m, 2H), 2.01 (m, 2H), 3.17 (s, 9H), 3.41 (m, 2H), 3.72 (t, J = 6 Hz, 2H); mass spectrum m/e (rel intensity) 100 (0.3), 59 (10.7), 58 (100), 50 (35.0), 42 (25.3).

Anal. Calcd for $C_7H_{17}Cl_2N$: C, 45.17; H, 9.21; N, 7.53. Found: C, 44.77; H, 9.38; N, 7.79.

5-Chloro-n-pentyltrimethylammonium chloride was prepared from 1,5-dichloropentane and trimethylamine at 60°C in methanol. The solvent was removed by rotary evaporation and the resulting white solid was washed several times with diethyl ether, filtered and dried under vacuum: mp 115-116°C; 400 MHz ^{1}H nmr data (CD_3CN) δ 1.56 (m, 2H), 1.88 (m, 4H), 3.15 (s, 9H), 3.37 (m, 2H), 3.68 (t, J = 7 Hz, 2H); mass spectrum m/e (rel intensity) 151 (0.2), 149 (0.7), 114 (1.4), 59 (5.4), 58 (89.3), 42 (11.7), 36 (100).

Anal. Calcd for $C_8H_{19}Cl_2N$: C, 48.01; H, 9.57; N, 7.00. Found: C, 48.37; H, 9.67; N, 7.32.

4-Chloro-n-pentyltrimethylammonium chloride was prepared from 1,4-dichloropentane and trimethylamine at 50°C in methanol. The solvent was removed by rotary evaporation and the resulting white solid was washed several times with diethyl ether, filtered and dried under vacuum: mp 131-133°C; 400 MHz ^1H nmr data (CD_3CN) δ 1.52 (d, J = 7.2 Hz, 3H), 1.79 (m, 2H), 1.98 (m, 2H), 3.13 (s, 9H), 3.36 (m, 2H), 4.23 (m, 1H); mass spectrum m/e (rel intensity) 149 (0.1), 114 (0.1), 113 (1.1), 59 (6.3), 58 (100), 50 (17.6), 42 (15.1).

Anal. Calcd for $C_8H_{19}Cl_2N$: C, 48.01; H, 9.57; N, 7.00. Found: C, 47.79; H, 9.57; N, 7.05.

3-Chloro-n-pentyltrimethylammonium chloride was prepared from 1,3-dichloropentane and trimethylamine at 50°C in methanol. The solvent was removed by rotary evaporation and the resulting white solid was washed several times with diethyl ether, filtered and dried under vacuum: mp 154-155°C; 400 MHz ^1H nmr data (CD_3CN) δ 1.01 (t, J = 7.2 Hz, 3H), 1.81 (m, 2H), 2.21-2.33 (m, 2H), 3.15 (s, 9H), 3.49 (d of t, J = 12, 3.6 Hz, 1H), 3.65 (d of t, J = 12, 3.6 Hz, 1H), 4.04 (m, 1H); mass spectrum m/e (rel intensity) 114 (0.2), 113 (1.3), 59 (9.6), 58 (100), 50 (11.4), 42 (21.0).

Anal. Calcd for $C_8H_{19}Cl_2N$: C, 48.01; H, 9.57; N, 7.00.

Found: C, 47.98; H, 9.50; N, 6.99.

6-Chloro-n-hexyltrimethylammonium chloride was prepared from 1,6-dichlorohexane and trimethylamine at 50°C in methanol. The solvent was distilled from the reaction mixture at room pressure to yield an oily solid. The solid was dissolved in methylene chloride and precipitated with diethyl ether. The precipitated solid was dissolved in water and washed with methylene chloride three times. The water was removed by distillation under reduced pressure and the product was dried under vacuum: mp 92-93°C; 200 MHz ^1H nmr data (CD_3CN) δ 1.24-1.57 (m, 4H), 1.74 (m, 4H), 3.06 (s, 9H), 3.27 (m, 2H), 3.59 (t, J = 6 Hz, 2H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (3.9), 180 (37.4), 179 (12.3), 178 (100), 144 (5.5).

5-Chloro-n-hexyltrimethylammonium chloride was prepared from 1,5-dichlorohexane and trimethylamine at 50°C in methanol. The solvent was distilled from the reaction mixture at room pressure to yield an oily solid. The solid was dissolved in methylene chloride and precipitated with diethyl ether. The precipitated solid was dissolved in water and washed three times with methylene chloride. The water was removed by distillation under reduced pressure, and the product was dried under vacuum:

mp 64-65°C; 200 MHz ^1H nmr data (CD_3CN) δ 1.48 (d, J = 6 Hz, 3H), 1.73 (m, 6H), 3.12 (s, 9H), 3.37 (m, 2H), 4.12 (m, 1H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (3.5), 180 (34.3), 179 (11.3), 178 (100), 144 (3.5).

4-Chloro-n-hexyltrimethylammonium chloride was prepared from 1,4-dichlorohexane and trimethylamine at 50°C in methanol. The solvent was distilled from the reaction mixture at room pressure to yield an oily solid. The solid was dissolved in methylene chloride and precipitated with diethyl ether. The precipitated product was dissolved in water and washed three times with methylene chloride. The water was removed by distillation under reduced pressure, and the product was dried under vacuum: mp 117-120°C; 200 MHz ^1H nmr data (CD_3CN) δ 1.00 (t, J = 7 Hz, 3H), 1.75 (m, 4H), 2.02 (m, 2H), 3.05 (s, 9H), 3.29 (m, 2H), 3.96 (m, 1H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (3.6), 180 (33.9), 179 (11.3), 178 (100), 144 (5.0).

3-Chloro-n-hexyltrimethylammonium chloride was prepared from 1,3-dichlorohexane and trimethylamine at 50°C in methanol. The solvent was distilled from the reaction mixture at room pressure to yield an oily solid. The solid was dissolved in methylene chloride and pre-

cipitated with diethyl ether. The precipitated solid was dissolved in water and washed three times with methylene chloride. The water was removed by distillation under reduced pressure, and the product was dried under vacuum: mp 112-114°C; 200 MHz ^{1}H nmr data (CD_3CN) δ 0.95 (t, J = 7 Hz, 3H), 1.49 (m, 2H), 1.77 (m, 2H), 1.85 (m, 2H), 3.19 (s, 9H), 3.58 (m, 2H) 4.05 (m, 1H); fast atom bombardment mass spectrum m/e (rel intensity) 181 (4.0), 180 (38.7), 179 (12.9), 178 (100), 144 (10.0).

n-Butylchloromethyldimethylammonium chloride was prepared from n-butyldimethylamine and methylene chloride in methanol at 50°C. The solvent was removed by rotary evaporation and the resulting oily solid was washed with diethyl ether. The solid was dissolved in water and washed three times with methylene chloride. The water was removed by distillation under reduced pressure, and the product dried under vacuum: mp 108-110°C; 200 MHz ^{1}H nmr data (CD_3CN) δ 1.06 (t, J = 7 Hz, 3H), 1.45 (sext., J = 8 Hz, 2H), 1.81 (m, 2H), 3.36 (s, 6H), 3.62 (m, 2H), 5.65 (s, 2H); fast atom bombardment mass spectrum m/e (rel intensity) 153 (3.1), 152 (37.8), 151 (9.9), 150 (100), 116 (11.1).

Anal. Calcd for $C_7H_{17}Cl_2N$: C, 45.17; H, 9.21. Found: C, 45.22; H, 9.16.

n-Pentylchloromethyldimethylammonium chloride was prepared from n-pentyldimethylamine and methylene chloride in methanol at 50°C. The solvent was removed by rotary evaporation and the resulting oil was washed with diethyl ether. The solid was dissolved in water and washed three times with methylene chloride. The water was removed by distillation under reduced pressure, and the product dried under vacuum: mp 57-57.5°C; 200 MHz ^1H nmr data (CD_3CN) δ 1.02 (t, J = 8 Hz, 3H), 1.45 (m, 4H), 1.83 (m, 2H), 3.38 (s, 6H), 3.62 (m, 2H), 5.68 (s, 2H); fast atom bombardment mass spectrum m/e (rel intensity) 167 (3.1), 166 (33.1), 165 (9.9), 164 (100), 130 (14.1). Anal. Calcd for $C_8H_{19}Cl_2N$: C, 48.01; H, 9.59. Found: C, 48.39; H, 9.95.

n-Hexylchloromethyldimethylammonium chloride was prepared from n-hexyldimethylamine and methylene chloride in methanol at 50°C. The solvent was removed by rotary evaporation and the resulting oil was washed with diethyl ether. The solid was dissolved in water and washed three times with methylene chloride. The water was removed by distillation under reduced pressure, and the product dried under vacuum: mp 72-74°C; 200 MHz ^1H nmr data (CD_3CN) δ 1.01 (t, J = 7 Hz, 3H), 1.45 (m, 6H), 1.83 (m, 2H), 3.40 (s, 6H), 3.64 (m, 2H), 5.74 (s, 2H); fast atom

bombardment mass spectrum m/e (rel intensity) 181 (3.8), 180 (36.0), 179 (12.0), 178 (100), 144 (20.6). Anal. Calcd for $C_9H_{21}Cl_2N$: C, 50.47; H, 9.88. Found: C, 50.70; H, 9.96.

n-Pentyldimethylamine was prepared from 1-bromopentane and dimethylamine with sodium carbonate in 50:50 methanol:water v:v, at 60°C. The solution was extracted three times with diethyl ether and the extracts were dried over anhydrous sodium sulfate. The product was isolated by fractional distillation to yield a clear liquid: bp 118-122°C (692 mm) [lit.[82] bp 123°C]; n_D^{20} 1.4081 [lit.[82] n_D^{20} 1.4083]; 90 MHz ^1H nmr data (CD_3CN) δ 0.90 (t, J = 7 Hz, 3H), 1.33 (m, 6H), 2.20 (s, 8H).

n-Pentylmethylamine was prepared from 1-bromopentane and methylamine with sodium carbonate in water. The solution was extracted three times with diethyl ether and the extracts were dried over anhydrous sodium sulfate. The product was isolated by fractional distillation to yield a clear liquid: bp 47-49°C (60 mm) [lit.[83] 45-47°C (60 mm)]; 400 MHz ^1H nmr data (CD_3CN) δ 0.72 (t, J = 7 Hz, 3H), 1.19 (m, 4H), 1.54 (m, 2H), 2.69 (d, J = 6Hz, 3H), 2.95 (m, 2H), 5.97 (broad m, 1H) [lit.[83] δ 0.6 (s, 1H), 0.75-1.08 (m, 3H) 1.16-1.5 (m, 6 H), 2.38 (s, 3H), 2.4-2.72 (m, 2H)].

n-Hexylmethylamine was prepared from 1-bromohexane and methylamine with sodium carbonate in methanol:water 3:2 v:v, at 60°C. The solution was extracted three times with diethyl ether and the extracts were dried over sodium sulfate. The product was isolated by fractional distillation to yield a clear liquid: bp 32°C (4.7 mm) [lit.[77] 138-140°C (760 mm)]; n_D^{20} 1.4184 [lit.[77] n_D^{20} 1.4186); 400 MHz ^1H nmr data (CD_3CN) δ 0.69 (t, J = 7 Hz, 3H), 1.14 (m, 6H), 1.53 (m, 2H), 2.69 (d, J = 6 Hz, 3H), 2.94 (m, 2H), 5.97 (broad m, 1H).

N-Chlorodimethylamine was prepared following the procedure of Ingold.[32] Dimethylamine and 6% aqueous sodium hypochlorite were mixed together. The solution was extracted with three portions of diethyl ether, the ether fractions were combined, washed with water and dried over sodium sulfate. A slight excess of concentrated sulfuric acid (based on the dimethylamine used) was added and the ether was evaporated under vacuum in the dark. The resulting white crystals obtained were dissolved in an aliquot of 15% CD_3CO_2D/85% H_2SO_4 and stored in the dark at -78°C.

N-Chloro-n-hexylmethylamine and N-Chloro-n-pentylmethylamine were prepared by the method of Coleman.[2] The amine was stirred in a 50:50 mixture of ligroin and 3M

aqueous sodium hydroxide (v:v) at 0°C. Chlorine was purified by passing it through traps containing concentrated sulfuric acid, calcium sulfate and glass wool at such a rate as to maintain a positive pressure of 40 mm Hg. When fuming had ceased and the ligroin solution had turned faintly green, the chlorine flow was stopped and the ligroin layer was separated. The ligroin was washed with ice cold fractions of 3 N sodium hydroxide, water and 2 N sulfuric acid. The ligroin layer was allowed to sit for 10 minutes in 15% CD_3CO_2D/85% H_2SO_4 while kept ice cold, and another 20 minutes with occasional stirring. This solution was then immediatedly used in the chlorination studies investigated.

IV.4 Analytical Procedures

Photochlorination of Quaternary Ammonium Salts in Hexachloroacetone. A solution of the salt (0.012-0.018 M) in hexachloroacetone was prepared and aliquot portions (5×10^{-3} ℓ) placed in pyrex reaction ampoules. A solution of chlorine (0.024-0.035 M) in hexachloroacetone was prepared, quantitatively measured by iodometric titration with aqueous sodium thiosulfate solution and aliquot samples (5×10^{-4} ℓ) added to each ampoule. The ampoules were degassed three times by the freeze-thaw technique, sealed, equilibrated to 30°C and exposed to 2 x 100 watts

of incandescent light. After irradiation the tubes were opened and the solvent removed by vacuum distillation. Weighed amounts of naphthalene were added, the samples were dissolved in perdeuterioacetonitrile and analyzed as outlined in Appendix 1. All of the signals in the nmr spectrum could be accounted for either by starting material, observed products or known impurities in the solvent.

Photochlorination of Quaternary Ammonium Salts and n-Pentyldimethylamine in 15% CD_3CO_2D/85% H_2SO_4 with Molecular Chlorine. A solution of the salt (0.69-0.72 M) or amine (1.0 M) in the acid solvent was prepared and aliquot portions (1×10^{-3} ℓ) placed in pyrex reaction ampoules. A solution of chlorine (0.1 M) in the acid solvent was prepared, quantitatively measured by iodometric titration with aqueous sodium thiosulfate solution and aliquot samples (2×10^{-3} ℓ) added to each ampoule. The ampoules were degassed three times by the freeze-thaw technique, sealed, equilibrated to 30°C and exposed to 2 x 100 watts of incandescent light. After irradiation the tubes were opened and o-dimethoxybenzene (veratrole, weighed amounts) was added, and the samples analyzed as outlined in Appendix 1.

Photochlorination of Quaternary Ammonium Salts and n-Pentyldimethylamine in 15% CD_3CO_2D/85% H_2SO_4 with N-Chlorodimethylamine. A solution of the salt (0.36 M) or amine (0.36 M) in the acid solvent was prepared and aliquot portions (1×10^{-3} ℓ) placed in pyrex reaction ampoules. Aliquot samples (5×10^{-5} ℓ) of the previously prepared solution of N-chlorodimethylamine (1.0 M) in the solvent were added to each ampoule. The ampoules were degassed three times by the freeze-thaw technique, sealed, equilibrated to 30°C and exposed to 2 x 100 watts of incandescent light. After irradiation the tubes were opened and weighed amounts of veratrole were added, and the samples analyzed as outlined in Appendix 1.

Photochlorination of N-Chloro-n-pentylmethylamine and N-Chloro-n-hexylmethylamine in 15% CD_3CO_2D/85% H_2SO_4. An aliquot (3×10^{-3} ℓ) of the solution of N-chloroamine (0.62-0.7 M) in the acid solvent was placed in each pyrex reaction ampoule. The ampoules were degassed three times by the freeze-thaw technique, sealed, equilibrated to 30°C and exposed to 2 x 100 watts of incandescent light. After irradiation the tubes were opened and weighed amounts of veratrole were added, and the samples analyzed as outlined in Appendix 1.

Photochlorination of 1-Chlorobutane with N-Chlorodimethylamine in 15% CH_3CO_2H/85% H_2SO_4. A solution of 1-

chlorobutane (0.35 M) in the acid solvent was prepared and an aliquot (3×10^{-3} ℓ) of this solution was placed in each pyrex reaction ampoule. An aliquot sample (3×10^{-4} ℓ) of the previously prepared solution of N-chlorodimethylamine (0.98 M) in the solvent was added to each ampoule. The ampoules were degassed three times by the freeze-thaw method, sealed, equilibrated to 30°C and exposed to 2 x 100 watts of incandescent light. After irradiation the tubes were opened, added to ice-cold water and extracted with carbon tetrachloride. A standard solution of 1,5-dichloropentane in carbon tetrachloride was added and the mixture analyzed by Glpc. Glpc analysis was carried out using a 1/4" x 20' glass column of 5% SE 30 on Chromosorb W at a flow rate of 40 cc/min. and a temperature program from 30 to 120°C. The products were identified by a comparison of their retention times with those of authentic materials and the yields determined using the standard 1,5-dichloropentane. The yield was calculated by the following equation

$$\text{moles X} = \frac{\text{integration X}}{\text{integration Std}} \times \text{Cf} \times \text{moles Std}$$

where Cf is the calibration factor determined from the results obtained from the analysis of a standard calibration mixture prepared from known amounts of

authentic materials.

$$Cf = \frac{\text{moles X / moles Std}}{\text{area integration X / area integration Std}}$$

The Photochlorination of 2,3-Dimethylbutane in Hexachloroacetone and Carbon Tetrachloride with Molecular Chlorine. A solution of 2,3-dimethylbutane (1.5 M), solvent and Freon 112 (0.32 M, gc standard) was prepared and an aliquot sample (5.0×10^{-3} ℓ) placed in each pyrex reaction ampoule. A solution of chlorine (0.54 M) in the solvent used was prepared, its concentration measured by iodometric titration with aqueous sodium thiosulfate solution and aliquot samples (2.5×10^{-3} ℓ) added to each ampoule. The ampoules were degassed three times by the freeze-thaw technique, sealed, equilibrated to 30°C and exposed to light. After irradiation the tubes were opened, and analyzed by Glpc.

Glpc analysis was carried out using a 1/4" x 20' glass column of 10% Ucon 50 HB5100 on Chromosorb WAW at a flow rate of 20 cc/min. and a temperature of 80°C. The products were identified by comparison of their retention times with those of authentic materials and the yields determined by using the standard Freon 112 as described for the experiment with 1-chlorobutane.

The Photochlorination of 2,3-Dimethylbutane in 15% CH_3CO_2H/85% H_2SO_4 with Molecular Chlorine. Aliquot samples (1.6×10^{-4} ℓ) of 2,3-dimethylbutane and a solution of chlorine (0.06 M) in 15% CH_3CO_2H/85% H_2SO_4 (2.0×10^{-3} ℓ) were placed in pyrex reaction ampoules. The ampoules were degassed three times by the freeze-thaw technique, sealed, equilbrated to 30°C and irradiated for the requisite amount of time. After irradiation the tubes were frozen, opened and diluted with ice-cold water. The aqueous solution was washed three times with CCl_4 and the CCl_4 solution was analyzed by Glpc as described for the reactions in hexachloroacetone and CCl_4.

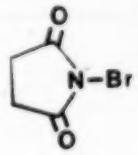
Product Stability Experiment. n-Pentyltrimethylammonium chloride was chlorinated in hexachloroacetone at 30°C and analyzed as described previously. The nmr solvent (CD_3CN) was allowed to evaporate and each sample was dissolved in the appropriate amount of 15% CD_3CO_2D/85% H_2SO_4 and placed in stoppered pyrex flasks. The flasks were irradiated at 30°C for the same length of time as was used for the chlorination reactions carried out in the acid solvent. The mixtures were analyzed as described previously. Within the limits of the experimental error (±5%) the ratio of products were unchanged.

PART 2

INTRODUCTION

V.1 Background

As a class of halogenating agents, N-haloamines have exhibited only limited utility for synthetic purposes. By far the most widely used N-halo-reagents are the N-haloimides. The major advantage of these halogenating reagents is their ability to be used in neutral organic solvents, although they have only a limited solubility. The most extensively studied and best known of the N-haloimides is N-bromosuccinimide or NBS (27).



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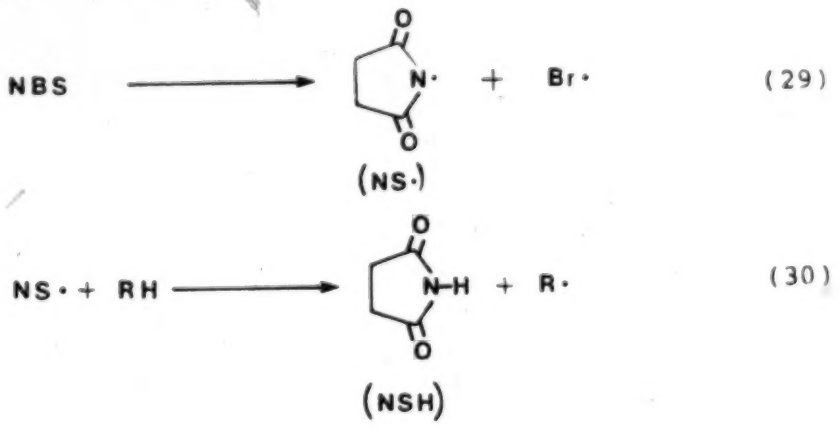
The first reports of a method for introduction of a halogen in the allylic position of an olefin were those of Wohl.[84,85] The reagent used was N-bromoacetamide. The method did not receive widespread use until the 1940's however, due to the lack of availability of the brominating reagent. Ziegler and coworkers in 1942[86] improved the technique and introduced the new reagent NBS. This procedure gave very good yields of olefin

brominated in the allylic position, and with the easily prepared NBS the method became widely used and known as the Wohl-Ziegler reaction (for a review to 1948 see Djerassi[87]).

Substitution of an allylic hydrogen by a halogen, with little or no addition to the olefin, was not a commonly encountered reaction, and the report generated a great amount of interest in the mechanism of this transformation. The first mechanism proposed was that of Bloomfield in 1944.[88] Since the reaction involved allylic bromination, and very little addition of bromine to the olefin (with molecular bromine, addition to the olefin is almost the exclusive product), a radical chain mechanism, Scheme IV, was proposed which involves abstraction by a succinimidyl radical rather than by a bromine atom.



Scheme IV

An alternative mechanism, based on results obtained for N-chlorosuccinimide was suggested by Goldfinger and coworkers.[89] This mechanism was later proposed for bromination of olefins and toluenes with NBS by Sixma and Riem.[90] The Goldfinger mechanism is shown in Scheme V.

$$NBS \longrightarrow NS\cdot + Br\cdot \qquad (29)$$

$$Br\cdot + RH \longrightarrow R\cdot + HBr \qquad (32)$$

$$HBr + NBS \longrightarrow NSH + Br_2 \qquad (33)$$

$$R\cdot + Br_2 \longrightarrow RBr + Br\cdot \qquad (34)$$

Scheme V

Goldfinger argued that a halogen atom in the presence of an olefin would behave in two different manners depending upon its concentration. In the case of bromine the addition to an olefin (Scheme VI) was proposed to involve two bimolecular reactions, the first of which is reversible.

$$Br\cdot + \rangle C{=}C\langle \rightleftharpoons Br{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}\cdot \qquad (35)$$

$$Br{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}\cdot + Br_2 \longrightarrow Br{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}Br + Br\cdot \qquad (36)$$

Scheme VI

The NBS, through the ionic reaction with hydrogen bromide (equation 33), was proposed to be a steady source of a low concentration of molecular bromine. Due to the irreversibility of the hydrogen abstraction sequence, and the reversible addition of bromine atoms to the olefin (equation 35), the allylic bromination was suggested to be favored over addition under these conditions. The addition of bromine to the olefin was proposed to be favored only under conditions of high concentrations of molecular bromine.

No experimental evidence was available to distinguish between these two mechanisms at the time the Goldfinger mechanism was proposed. Sixma and Riem[90] favored the Goldfinger mechanism based on results they obtained with cyclohexene and methyl crotonate. They found, using low concentrations of molecular bromine, that these two olefins could be brominated allylically. Tedder and McGrath[91] confirmed the results of Sixma and Riem with cyclohexene. They also noted that the Goldfinger mechanism implies several additions to and dissociations from the olefin by bromine atoms, before allylic abstraction occurs. To investigate this the bromination of cis-3-hexene was carried out with NBS. If the Goldfinger mechanism were correct the unreacted olefin recovered should be partially isomerized to trans

via an addition-rotation-elimination sequence. When the unbrominated 3-hexene was recovered and analyzed it was found to be 85% trans.[91] Kooyman and coworkers[92] had previously shown that in N-chlorosuccinimide (NCS) chlorinations the NCS behaved as a source of a low concentration of molecular chlorine, and that a chlorine atom was the abstracting species.

In 1963 three groups reported further evidence supporting the Goldfinger mechanism. Martin[93] and Russell[94] reported preliminary results from competitive brominations of a variety of substrates with NBS which showed similar relative reactivities to those observed with molecular bromine. Based on these results they supported the Goldfinger mechanism as the correct one. Walling, Rieger and Tanner[95] studied the relative reactivity of various substituted toluenes, as did Martin,[93,98] to NBS and to molecular bromine. The log of the relative reactivities versus the σ^+ substituent constant for each substituted toluene was plotted, using the reactivity of toluene as a reference. A ρ value of -1.38 with a correlation of 0.977 was obtained, which agreed well with the value of $\rho = -1.36$ obtained by Martin[93] for molecular bromine under conditions of high $[Br_2]/[HBr]$. Comparison of the relative reactivities of various other hydrocarbons with NBS or with molecular

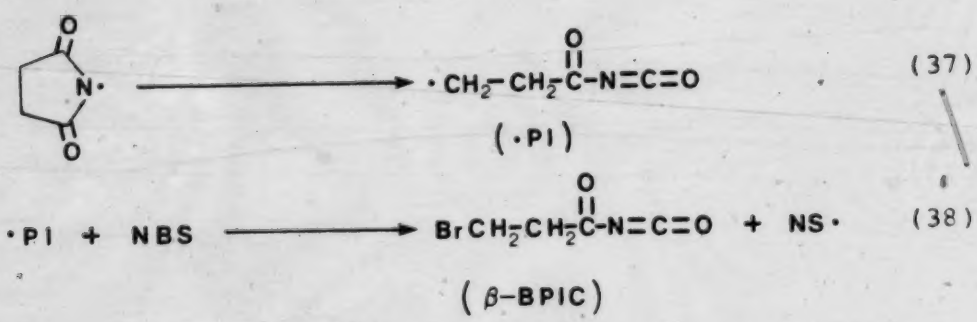
bromine also indicated that the same abstracting species was involved in the two reagents. Walling and Rieger[96] also prepared several N-bromohydantoins and N-bromoacetamide. Their relative reactivities with substituted toluenes were shown to correlate with σ^+ substituent constants, with ρ values between -1.10 and -1.36 and were thus concluded to react by the Goldfinger mechanism. Russell[97] and Martin[98] both published the complete results of their studies with NBS and hydrocarbons at the same time as those of Walling and coworkers. Russell and Desmond showed that the relative reactivity of NBS in dichloromethane (where the reagent is soluble) with various α-substituted toluenes was the same as could be obtained with molecular bromine in carbon tetrachloride. Martin and Pearson plotted the log of the relative reactivities of substituted toluenes versus σ^+ substituent constants for NBS, N-bromotetrafluorosuccinimide (NBTFS), N-bromotetramethylsuccinimide (NBTMS) and molecular bromine. At 80°C the ρ values for NBS, NBTFS, NBTMS and Br_2 were -1.46, -1.45, -1.36 and -1.36. At 19°C the ρ values for NBTMS and Br_2 were -1.79 and -1.76. At one temperature the ρ values for a succinimidyl radical and bromine atoms might be fortuitously similar, but obtaining the same ρ values at two different temperatures argued for a common abstracting species.

Also in the reactions of NBS and NBTFS it was not likely that the nitrogen centered radicals obtained from these two reagents should have highly similar polar requirements. Both groups came to the conclusion that bromine atoms were the abstracting species involved in NBS brominations.

The possibility that some situations existed where reactions could be attributed to succinimidyl radicals, however was not ignored. Russell and Desmond[97] also investigated the relative reactivities of several cyclic olefins with NBS, and noted that these reactions went more slowly than those with the substituted toluenes. Russell suggested that the olefins served to trap the molecular bromine and bromine atoms, such that succinimidyl radicals could be the abstracting species for these reactions. This would appear to support the Bloomfield mechanism for allylic bromination, but an important difference was the choice of solvent used. For the Wohl-Ziegler reaction carbon tetrachloride, in which molecular bromine is soluble but NBS is not, is the solvent used. In Russell's work however, he used methylene chloride with NBS concentrations which were soluble such that both NBS and molecular bromine were dissolved in the solution.

Johnson and Bublitz[99,100] and Martin and Bartlett[101]

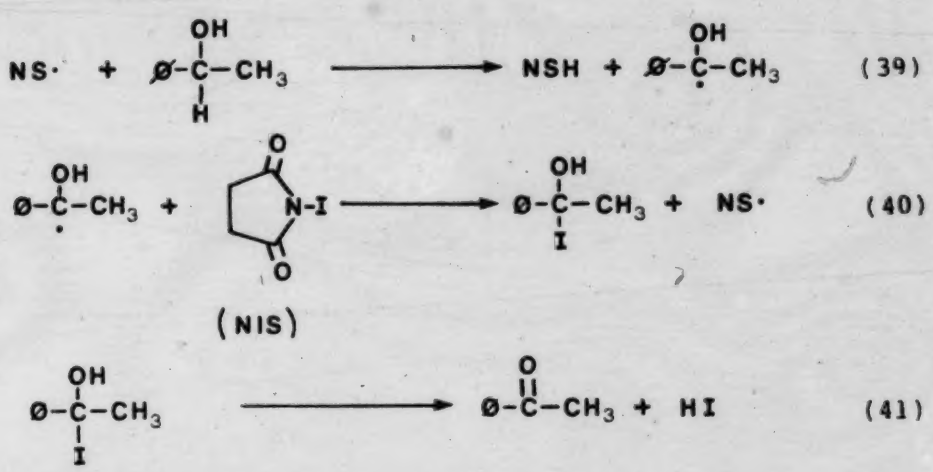
produced the first results indicating the presence of succinimidyl radicals in solution. Johnson and Bublitz[99] first observed the production of β-bromopropionyl isocyanate (β-BPIC) from NBS in refluxing chloroform with benzoyl peroxide and various allylic compounds. They later[100] broadened the choice of solvents in which the product could be formed. Martin and Bartlett[101] explained the formation of β-BPIC as coming from a β-scission rearrangement of succinimidyl radicals as shown in Scheme VII.



Scheme VII

In 1969 Beebe and Howard[102] proposed the involvement of succinimidyl radicals in the oxidation of 1-phenylethanol with N-Iodosuccinimide (Tanner[103] had previously suggested a hydrogen abstraction by a protonated succinimidyl radical in the reaction of N-Iodosuccinimide in trifluoroacetic acid). Since iodine did not produce the

oxidation of the alcohol, and the influence of radical initiators and inhibitors indicated a radical mechanism, the mechanism of Scheme VIII was suggested. The conclusion that succinimidyl radical rather than the



Scheme VIII

β-propionyl isocyanate radical (·PI see equation 37) was the abstracting species was supported by 80-90% yields of succinimide.

Martin and Incremona[104] were prompted by this observation to investigate further the mechanism of NBS with allylic compounds in refluxing benzene. They found identical relative reactivities for allylic abstraction by molecular bromine, NBS, and N-bromotetramethylsuccinimide. N-bromotetrafluorosuccinimide exhibited a higher selectivity than the other reagents, but this was

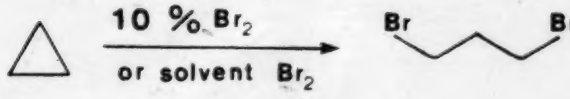
shown to be due to ionic addition to the olefin followed by elimination of tetrafluorosuccinimide and an ionic rearrangement to the product allylic bromide.

Since the Goldfinger mechanism had become accepted as the mechanism operating for brominations by NBS, and since equation 33 allowed rapid removal of HBr from the reaction mixture, brominations using NBS with added molecular bromine were suggested by Tanner[105] to be a method to obtain bromine atom selectivities uncomplicated by hydrogen bromide reversal (equation 42). Involvement

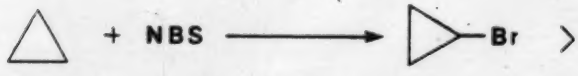
$$R\cdot + HBr \longrightarrow RH + Br\cdot \qquad (42)$$

of HBr reversal in brominations with molecular bromine meant that observed product ratios were not necessarily true indicators of the selectivities for hydrogen abstraction. Tanner and coworkers[106,107] observed changing selectivities with percentage reaction in the NBS bromination of 1-bromobutane and cyclohexylbromide. The change was suggested to be due to incomplete scavenging of HBr at the final stages of the reaction where NBS is almost completely reacted. Traynham and coworkers[108] confirmed these observations, however the variation in behavior was not included in their evaluation of the proposed mechanism for the NBS bromination of alkanes.

Traynham and Lee[109] presented results in 1974 which they proposed to support the Bloomfield mechanism for NBS brominations under certain conditions. Based upon a comparison of the relative reactivities of various alkanes and alkyl halides with NBS or with molecular bromine in solvent acetonitrile they came to the conclusion that the chain carrying species was not the same for these two reagents. The most striking example was the bromination of cyclopropane (equations 43 and 44). The two reagents gave two different products



(43)



(44)

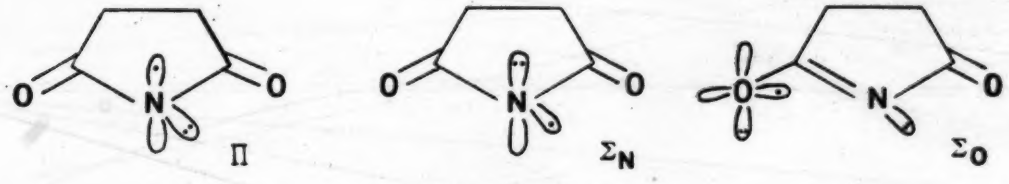
indicating that bromine atoms are not involved in the reaction with NBS. Based on these results they proposed that with NBS a succinimidyl radical chain operates (the Bloomfield mechanism) for abstraction from alkanes, but that a bromine atom chain governs the reaction during benzylic halogenation (previously reported).[93-98]

Skell, Lindstrom and Day[110] presented a method to insure a succinimidyl radical chain for NBS brominations in 1974. Walling and coworkers[95,111] had previously used

small amounts of olefin in the reactions of NBS and with t-butylhypohalite reagents to trap halogen atoms and prevent their interference as abstracting species. In this manner they were able to observe the selectivity of the t-butoxyl radical uncontaminated by halogen atom selectivities. Skell proposed that by using solvents dichloromethane and acetonitrile (solvents in which NBS is soluble), and through addition of small amounts of ethylene as a trap for molecular bromine, it was possible to obtain NBS selectivities which were clearly different from those shown by molecular bromine uncomplicated by HBr reversal. The selectivities were shown to be similar to selectivities obtained for the reaction of the more energetic chlorine atom. When cyclohexene was allowed to react with NBS in carbon tetrachloride at reflux (Ziegler's method) only 3-bromocyclohexene was observed to be a product. When cyclohexene was brominated photochemically in acetonitrile with NBS, however, 15% of the products was 4-bromocyclohexene. Skell explained this as being due to the solubility of the NBS in the two solvents. In carbon tetrachloride, where NBS is insoluble, the concentration of bromine is high, relative to that of NBS, such that bromine atoms dominate the reaction even in the presence of the olefin. In acetonitrile, where NBS is soluble, the olefin serves to keep

the concentration of bromine low, relative to the now soluble NBS, such that succinimidyl radicals dominate the reaction.

In 1975 Koenig and Wielesek[112] used INDO calculations to estimate the first three states of the succinimidyl radical. They found, using C_{2V} symmetry and partial geometry optimization, that the ground state is a π configuration (see 28), the first excited state is a Σ_N configuration (see 29) and the second excited state is a Σ_O configuration (see 30). However, if the geometry was



28 29 30

slightly distorted asymmetrically from C_{2V} symmetry (the C-O bond was stretched by 0.02 A and the C-N bond was contracted by 0.04 A) the Σ_N state and the π state both increased in energy, but retained a similar energy separation. The Σ_O state however decreased to within ~6 kcal./mol. of the π state. Thus Koenig predicted that both the π and Σ_O state should be thermally accessible. He pointed out that the Σ_O and Σ_N states both correlate with the ground state of the isocyanate radical (·PI),

but the π state correlates with an excited state of •PI.

Later calculations have dealt only with the first two electronic states of the succinimidyl radical. Apeloig and Schreiber[113] used ab initio calculations to determine the energies of the first two electronic states. They used C_{2V} symmetry with complete geometry optimization and found the $\pi\ ^2B_1$ state (28) to be the ground state and the $\Sigma_N\ ^2A_1$ state (29) to be the first excited state. They estimated the energy separation between the two states to be 20-25 kcal./mol.

Clark[114] used MNDO calculations on N-chloro-succinimide (NCS) to predict which states of the succinimidyl radical would be formed by interaction with an alkyl radical or with a chlorine atom. He calculated the Σ_N state to be 13.8 kcal./mol. higher in energy than the π state. Using the MNDO optimum geometry he calculated the highest occupied molecular orbital (HOMO) to be the π^*_{N-Cl} orbital, and the lowest unoccupied molecular orbital (LUMO) to be a higher energy N-Cl antibonding orbital. The singly occupied molecular orbital (SOMO) of an electrophilic radical, such as a chlorine atom, was predicted to interact most strongly with the HOMO of NCS, in an orthogonal manner relative to the N-Cl bond. Reaction in this manner would yield the Cl-Cl bonding orbital and the π succinimidyl radical

SOMO. If the SOMO of the attacking radicals were to be high lying, such as for a primary alkyl radical, they were predicted to interact with the LUMO of NCS, in a colinear manner relative to the N-Cl bond. Reaction in this manner would yield the C-Cl bonding orbital and the Σ_N succinimidyl radical SOMO. Formation of the π radical by chlorine atom interaction was predicted to be exothermic by 14.6 kcal./mol. with an activation energy of 7.2 kcal./mol., and formation of the Σ_N radical by an alkyl radical ($\cdot CH_3$) was predicted to be exothermic by 0.8 kcal./mol. with an activation energy of 14.6 kcal./mol.

Dewar and coworkers[115] calculated the first two electronic states of the succinimidyl radical using UMNDO a spin-unrestricted version of MNDO. This method was said to be comparable to good ab initio calculations, and better than ones using minimum basis sets. Using this method they determined the ground state to be the π state and the next highest state to be the Σ_N state separated by an energy difference of 14.55 kcal./mol.

None of the theoretical studies done after Koenig's considered the Σ_O state. Koenig's results suggest that the ground state may not actually be the only state that is thermally accessible in solution. If the distorted geometry he considered is within a vibrational mode for

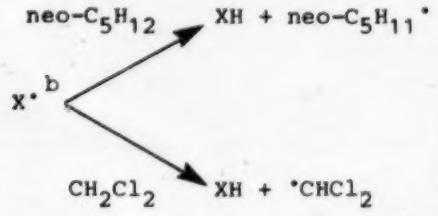
the radical it may be that the ground state is not the only state that is thermally accessible in solution, but rather a mixture of the π and Σ_0 states exists. Huzinaga, Klobukowski and Tanner[116] are presently in the process of carrying out a set of ab initio calculations on succinimidyl radical using a larger basis set. They are also looking at the effects of the possible deviations from C_{2V} symmetry (such as might occur in solution through collisions with the solvent molecules) on the energy separations between the electronic states.

An esr study of the succinimidyl radical has been reported recently.[117] A single crystal of succinimide was X-irradiated at 26°K to yield succinimidyl radicals. Based on coupling constants, the spin densities of 2s = 0.02 and 2p = 0.60 were determined with most of the remaining spin localized on the carbonyl oxygens. The minimum g value and maximum $a^{14}N$ were obtained at a direction perpendicular to the molecular plane. Based on these results they concluded the structure of the observed radical to be that of the π state.

The most recent addition to the debate over the mechanism of NBS bromination is the proposal of Skell that two chemically distinguishable states of succinimidyl radical in solution are possible, and necessary to

explain the reactivities observed.[118-124] Skell first proposed the possibility that two electronic states were necessary in a study of the competitive halogenation of neopentane and dichloromethane.[119] The results upon which he based this proposal are given in Table XI. The results presented indicate three different values of relative reactivity/H, r, for the competitive abstraction from the two substrates were obtained. With NBS and olefin, conditions which were supposed to prevent the involvement of molecular bromine, a high value of 21.3±2.0 was obtained. NBS in the presence of added bromine gave a moderate value of 1.15±0.16 and molecular bromine gave a low value of 0.1. Based on these results three radicals were proposed to be necessary. The high value in the presence of olefin (21.3) was proposed to be the selectivity of an excited state succinimidyl radical designated as σ (equivalent to either Σ_N or Σ_O), the moderate value in the presence of molecular bromine (1.15) was proposed to be due to the selectivity of a ground state succinimidyl radical designated as π and the low value obtained with molecular bromine (0.1) said to be the selectivity of a bromine atom. Further evidence in support of the conclusion that the value obtained from NBS with added molecular bromine was due to a succinimidyl radical was the fact that NIS with iodine gave the

Table XI. The Relative Reactivity/H of Neopentane and Dichloromethane with the NBS Reagents.[a]



Reagent (no. of experiments; % yields)	$(k_{neo-C_5H_{12}}/k_{CH_2Cl_2})$/H (r)
NBS-olefin (2; 4)	21.3 ± 2.0
NBS-Br_2 (6; 14-96)	1.15 ± 0.16
NIS-I_2 (4; 1-6)	1.15 ± 0.12
Br_2. (1; 3)	0.1

a. Taken from reference 119.
b. X· is the abstracting species.

same value (1.15). The nonenergetic iodine atoms could not be considered as an abstracting species.

The selective formation of the two electronic states was rationalized as follows. Based on the energy separation predicted by Koenig,[112] Skell proposed that the interaction of an alkyl radical with NBS (see equation 32) would be exothermic by ~20 Kcal./mol. and that this energy produced an exçited σ-state of the succinimidyl radical. Interaction of a bromine atom with NBS (equation 45) was approximately thermoneutral and thus

$$Br\cdot + NBS \longrightarrow NS\cdot + Br_2 \qquad (45)$$

could only produce the ground π-state of the succinimidyl radical. Further evidence was reported which was based on Koenig's proposal that only the Σ_N or the Σ_O states correlated with the ring opened radical, ·PI (see equation 37). In the presence of olefins 50-70% of the NBS was said to produce β-BPIC in agreement with assignment to the σ-state, however in the presence of bromine or iodine no isocyanates could be detected. The absence of β-BPIC was likewise in agreement with the assignment of the reactivities obtained with the NXS-X_2 reagents to the π-state. Based on these results Skell ascribed the addition reactions of NBS with various olefins[118] to be those of a σ-succinimidyl radical.

In two following reports Skell[120,121] repeated the results mentioned above and presented added evidence. The ring-opening reaction (equation 37) was proposed to be reversible based on results obtained with cis-2,3-dideuterio-N-chlorosuccinimide.[120] When the 2,3-dideuteriosuccinimide product was analyzed it was found to be a mixture of the cis- and trans-isomers. The isomerization of the succinimide moiety suggested that β-scission to the propionyl isocyanate radical had occurred, followed by rotation and ring closure (the reverse of β-scission reaction 37).

The limiting conditions under which the ring opening reaction occurred were more completely defined by Skell in 1982.[122] The yield of β-BPIC was shown to be directly proportional to the concentration of NBS in solution. This was suggested to be due to the reversibility of the ring opening reaction (equation 37). By decreasing the NBS concentration the rate of reaction with •PI to form β-BPIC (equation 38) is decreased, leading to reduced yields of β-BPIC since the rate of abstraction of solvent hydrogen atoms by the succinimidyl radical and the rate of ring closure of •PI to succinimidyl radical remain constant. The yield of β-BPIC was shown to be essentially independent of olefin concentration. Limiting conditions for the study of the π-radical were also outlined.

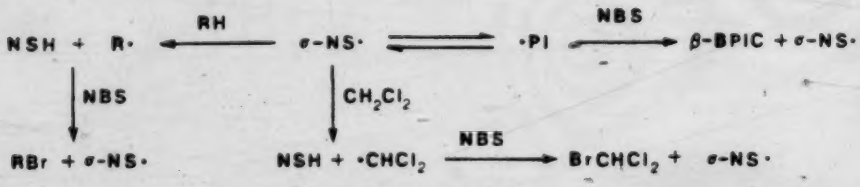
It was proposed that concentrations of molecular bromine greater than 10^{-3} M with NBS ensured generation of only the π-succinimidyl radical, since no β-BPIC was detected under these conditions. An in-between region, of bromine concentration 0 to 10^{-3} M, was said to exist where mixed reactivities (σ- and π-radical reactivities) would be observed. The quantum yield for photochemical initiation of the π-succinimidyl chain was estimated to be 7-9 mol./einstein and 63 mol./einstein for the σ-succinimidyl chain. It should be clear that the chain length estimated for these reactions must be almost entirely for the ring opening process.

In an accompanying report[123] Skell proposed a kinetic argument to differentiate between the reactivity of the π- and σ-succinimidyl radicals. Since both states were believed to be able to abstract a hydrogen atom from dichloromethane and ultimately yield bromodichloromethane, but only the σ-succinimidyl radical could lead to ring opened product, it was proposed that a measure of the involvement of the two states would be the ratio of $[BrCHCl_2]/[\beta\text{-BPIC}]$. The suggestion was also made that the π-succinimidyl radical could not only be formed by transfer of a bromine atom with NBS, equation 45, but could also be produced by transfer of a stabilized carbon-centered radical, $R_S^{\bullet}$, ($^{\bullet}CCl_3$, allylic, benzylic,

and 3°-alkyl), equation 46. If dichloromethane was

$$R_s\cdot + NBS \longrightarrow \underset{(\pi)}{NS\cdot} + R_sBr \qquad (46)$$

brominated by NBS under conditions designed to promote the formation of the σ-succinimidyl radical (added olefin) and a series of substrates were added, which upon reaction generate a stable radical, then the ratio of $[BrCHCl_2]/[\beta\text{-BPIC}]$ would change if more than one succinimidyl radical were involved. If instead only one succinimidyl radical were present, the σ-, then the ratio of products would remain constant, since the added substrate would react with succinimidyl radicals, but could not change the ratio of abstraction from dichloromethane to ring opened product, see Scheme IX.



Scheme IX

The results obtained are presented in Table XII. The hypothesis that two succinimidyl radicals were involved appeared to be substantiated, since the reported values of the ratio of products, $[BrCHCl_2]/[\beta\text{-BPIC}]$, obtained from the brominaton reactions of the NBS-vinyli-

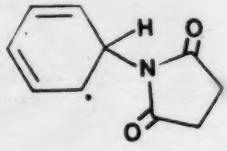
Table XII.[a] Competition Reactions of NBS-olefin with a Series of Substrates R_1H and CH_2Cl_2.[b]

Expt.	R_1H	$[BrCHCl_2]/[\beta\text{-BPIC}]$	Radical Product (R·)
1	---	0.024	$\cdot CHCl_2$
2-4	neo-C_5H_{12}	0.021	1°
5-6	n-butane	0.021	1°, 2°
7	cylopentane	0.025	2°
8	isobutane	0.037	1°, 3°
9	2,3-dimethylbutane	0.045	1°, 3°
10	cyclohexene	0.073	2°, allylic
11	benzene (0.2 M)	0.138	allylic
12	benzene (0.4 M)	0.294	allylic
13	benzene (0.78 M)	0.609	allylic
14	benzene (2.47 M)	>2.2[c,d]	allylic
15	benzene (2.30 M) neopentane	>1.4[c,d]	allylic, 1°
16	benzene (2.47 M) 1,3-butadiene	>0.78[c]	allylic
18	$CHCl_3$	>5.00[e]	$\cdot CCl_3$
-	1,3-butadiene	>0.32[c]	allylic

a. Data taken from reference 123.
b. Olefin added was CH_2CCl_2.
c. A minimum value since no β-BPIC was detected.
d. 3,3-Dimethyl-1-butene was used as olefin.
e. $[BrCCl_3]/[\beta\text{-BPIC}]$.

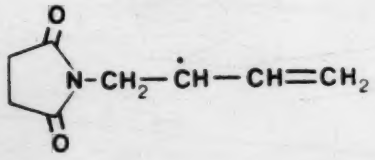
dine chloride reagent with substrates dichloromethane or dichloromethane and added neopentane, n-butane, or cyclopentane were all constant (0.022±0.002), while the substrates which generated stable radicals appeared to yield ratios of products which depended upon the substrate used, see Table XII.

The reactions run with added benzene showed product ratios, $[BrCHCl_2]/[\beta\text{-BPIC}]$, which were dependent upon the concentration of benzene, and were suggested to be due to transfer of NBS with the stable cyclohexadienyl radical, 31, which only formed the π-succinimidyl radical (see equation 46). In the reaction run with added 1,3-



31

butadiene the allylic radical, 32, formed from addition



32

of succinimidyl to 1,3-butadiene, was proposed to be too stable to form σ-succinimidyl through transfer with NBS,

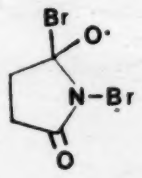
since no β-BPIC was detected. When NBS was reacted with chloroform no β-BPIC was detected which was explained by the trichloromethyl radical, 33, being stable enough that

$$\cdot CCl_3$$
33

transfer with NBS could only produce the π-succinimidyl radical (see equation 46).

Walling and coworkers[125] challenged the interpretations of Skell on the basis of the results of a kinetic study. They attempted to repeat Skell's initial results[119] with neopentane and dichloromethane, but could only estimate the amount of brominated material when the NBS brominations were carried out with added olefin. Little or no $BrCHCl_2$ was detected, and only a value of $r > 20$ could be assigned to the reactivity of the reagent under these conditions, since it was determined that with the concentrations used $r = 17$ could have been measured. When the reagent, NBS-Br_2, was used the r values obtained were variable, ranging from 1.0 to 2.5, and no β-BPIC was detected. Brominations with molecular bromine showed values of r ranging from 0.02-0.09. Although the previous results could not be duplicated it was conceded that they were in general agreement with those reported by Skell. The rate constants estimated

for hydrogen abstraction from methylene chloride were approximated as 55, 5.8 and 0.5 for the NBS-Br_2, NBS-olefin and molecular bromine reagents respectively. It was concluded that the rate observed for the NBS-olefin reagent was inconsistent with a rate which would be expected for an excited state radical. This conclusion was enforced by the observation that deuterium isotope effects, calculated from the product ratios obtained from the competitive brominations of perdeuteriodichloromethane and dichloromethane using the NBS-Br_2 and NBS-olefin reagents, were found to be (k_H/k_D) equal to 10.6 and 10.5 respectively. This similarity of these values was also inconsistent with the reactivity expected for two energetically very dissimilar species. Based on the r values obtained for reaction of the three reagents with neopentane and dichloromethane they agreed with Skell that three abstracting species must be involved. Considering their kinetic results, however, they proposed an alternative explanation for the observed values concluding that the NBS-olefin reagent involved a ground state succinimidyl radical and the NBS-Br_2 reagent involved a complex radical such as 34 or 35. A final observation



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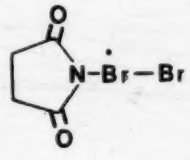


35

was made which was contrary to that observed by Skell.[123] When the bromination of chloroform was carried out using the NBS-olefin reagent an 80% yield of β-BPIC was reported. Skell had reported that no β-BPIC was formed, since chloroform was one of the substrates which produced a stable carbon-centered radical.

Skell produced an additional method for generation of π-succinimidyl radical, and criticized the results obtained by Walling in an appendix to his publication.[124] The new procedure for generation of π-succinimidyl radical involved running the reaction in dichloromethane in the presence of olefin and adding bromotrichloromethane such that the ratio $[BrCCl_3]/[CH_2Cl_2] \geq 0.32$. The olefin was to ensure that molecular bromine participation was excluded, and the quantity of bromotrichloromethane was made large enough to ensure that alkyl radicals (R·) were trapped by $BrCCl_3$ and not NBS (see Scheme X). The $\cdot CCl_3$ radical was said to be stable

$$\underset{(\pi)}{NS\cdot} + RH \longrightarrow NSH + R\cdot \qquad (30)$$

$$R\cdot + BrCCl_3 \longrightarrow RBr + \cdot CCl_3 \qquad (47)$$

$$NBS + \cdot CCl_3 \longrightarrow BrCCl_3 + \underset{(\pi)}{NS\cdot} \qquad (48)$$

Scheme X

enough that only the π-succinimidyl was formed by equation 48.

In criticizing the conclusions of Walling,[125] Skell presented k_H/k_D results which he had obtained. He found, using mixtures of perdeuteriodichloromethane, dichloromethane and molecular bromine, an abstraction ratio k_H/k_D = 11.53±0.12 for bromine atoms free from HBr reversal, equation 42 (addition of NBS or K_2CO_3 to trap HBr). Using his new method for generation of π-succinimidyl he obtained k_H/k_D = 5.85±0.08 and under σ-succinimidyl conditions he obtained k_H/k_D = 1.49±0.02. He claimed the k_H/k_D = 10.5 for NBS/Br_2 obtained by Walling was a ratio for bromine atoms since Walling used too much Br_2 relative to NBS. Skell could not explain Walling's k_H/k_D = 10.6 for NBS/olefin. Skell dismissed the kinetic results obtained by Walling saying that because of impurities present, the rate constants obtained from absolute rates were unreliable. The conflict in the results obtained with NBS/olefin in chloroform by Walling were explained as being due to the method used to degas the reaction mixture. Walling degassed his samples by flushing the solution with argon and capping the sample tube. Skell claimed this method did not remove oxygen sufficiently, but if the samples were degassed by multiple freeze-thaw cycles and sealing the tubes (as Skell did), then no β-

BPIC was formed in these reactions. No explanation however, was suggested by Skell as to how oxygen produced β-BPIC from π-succinimidyl radicals.

V.2 Proposal

After more than 30 years of investigation the mechanism of bromination by NBS is still a matter of some controversy. Even during the last 10 years results have appeared which were reinterpreted at a later date due to the complex variety of reaction steps possible. A completely clear picture of the conditions of solvent choice, substrates and additives, such that predictable reactivities are obtained, is still only partially defined.

The mechanistic conclusions which led to the suggestion that two chemically distinguishable states of the succinimidyl radical (π and σ) could exist in solution were consistent with the data presented, however the suggested mechanism for their generation was unique.

The reactions of NBS in benzene[126] have been shown to be quite complex with various products being formed. At the time of the original suggestion of the two chemically distinguishable states of succinimidyl radical we had obtained results for the bromination of

cyclopentane and cyclohexane with NBS[127] (at that time unpublished) which suggested an alternative explanation for the reactivities observed. Because of the novelty of the mechanistic proposals of Skell and the results obtained by this group it was felt to be important to address this problem further.

RESULTS

VI.1 Photobromination of Cyclohexane and Cyclopentane with NBS.

Brominations with NBS have been run under a variety of conditions depending on the source of initiation, choice of solvent, and additives used to ensure domination of one radical chain. The solvents most commonly used are Freon 113, carbon tetrachloride, benzene, dichloromethane, and acetonitrile. The first two solvents have been used because they limit complications of the mechanism through products arising from solvent. The latter three solvents have been chosen in preference to the first two because NBS is soluble in acetonitrile and dichloromethane, and slightly soluble in benzene.

To investigate the role of the solvent, two substrates, cyclohexane and cyclopentane, were brominated with NBS in Freon 113, benzene, dichloromethane, and acetonitrile. The relative rate constants k_5/k_6 ($k_{cyclopentane}/k_{cylohexane}$) were calculated using equation 49. The conditions and the results obtained are

$$k_5 / k_6 = \frac{[C_5H_9Br]}{[C_6H_{11}Br]} \cdot \frac{[C_6H_{12}]^o}{[C_5H_{10}]^o} \qquad (49)$$

given in Table XIII.

To ensure the dominance of bromine atoms as the chain propagating species, small amounts of bromine have been added.[106] Table XIV gives the conditions and results obtained from the photobromination of cyclopentane and cyclohexane using molecular bromine or NBS with added amounts of bromine. The addition of molecular bromine has little effect on the ratio k_5/k_6 in solvents Freon or benzene, however in dichloromethane and acetonitrile addition of molecular bromine increases the ratio k_5/k_6 to higher values, and eventually to those obtained in Freon and benzene. The values of vapor phase bromination and liquid phase bromination with molecular bromine are also given in Table XIV.

To limit the involvement of bromine atoms as the chain propagating species, small amounts of olefin which lack an allylic hydrogen (eg. ethylene, vinylidene chloride, and tert-butylethylene) can be added to the reaction mixture.[96,110] Addition of ethylene lowers the ratio k_5/k_6 in solvents dichloromethane or acetonitrile to values similar to those obtained without any additives, and carried out to low percentage conversion of NBS. In Freon the ratio k_5/k_6 is lowered dramatically to a similar value. The conditions used and results obtained from the photobromination of cyclopentane and cyclohexane with NBS/ethylene are given in Table XV.

Table XIII. The Effect of Solvent on the Relative Rates of Bromination of Cyclohexane (k_6) and Cyclopentane (k_5) with NBS (23°).

Solvent[c]	Reactants, mol/ℓ x 10^1			% Reaction[b]	k_5/k_6[a]
	$[C_5H_{10}]$	$[C_6H_{12}]$	[NBS]		
Freon 113	7.15	9.80	0.498	76	9.94
	7.98	8.10	0.508	49	9.44
Benzene[d]	5.15	5.49	0.331	100	9.16
	8.02	8.02	0.512	66	8.24
Methylene Chloride	5.09	4.77	0.395	100	1.78±0.04(3)
	4.91	5.04	0.405	39	1.04
Acetonitrile	7.03	7.59	0.511	100	1.12
	8.00	7.96	0.494	64	0.95
	7.10	7.58	0.437	50	0.79
	7.03	7.59	0.511	43	0.76

a. The numbers in parenthesis are the numbers of independent experiments. The errors are the average errors from the mean value listed.

b. Percentage reaction was determined by titration for active halogen prior to glpc analysis.

c. In two of the solvents, acetonitrile and Freon, a faint color of bromine developed during the course of the reaction. After titration with thiosulphate the color was discharged.

d. The absolute yield of brominated cycloalkanes was very low (~2.2% for cyclopentyl bromide and ~0.3% for cyclohexyl bromide). No dibrominated product was detected, since most of the NBS reacts by addition to solvent (see references 122 and 126).

Table XIV. The Effect of Added Bromine on the Relative Rates of Bromination of Cyclopentane (k_5) and Cyclohexane (k_6) with NBS (23°) in a Variety of Solvents.

Solvent	Reactants mol/ℓ x 10^3				Products, mol/mol of NBS reacted x 100			Mass Balance (%)[d]		k_5/k_6[e]
	$[C_5H_{10}]$	$[C_6H_{12}]$	[NBS]	$[Br_2]$[b]	NSH	B-BPIC	RBr[c]	NS-	Br-	
Br_2[a]	0.60	0.604	-	140-180						9.20±0.28
Vapor[a]	$1.2x10^{-4}$	$6.5x10^{-4}$	-	$47x10^{-4}$						9.66±0.26
Freon 113	7.15	9.80	0.498	-	-	-	-	-	-	9.94[f]
	5.96	8.16	0.417	$4x10^{-2}$	-	-	-	-	-	10.1
Benzene	5.15	5.46	0.331	-	-	-	-	-	-	9.16[f]
	4.28	3.94	0.446	$11x10^{-2}$	-	-	-	-	-	11.2±0.5 (2)
Methylene Chloride	8.10	8.21	1.03	-	56.5±1.4	38.9±3.2	53.8±0.3	95.4±4.6	92.7±3.5	1.77±0.01 (3)
	4.27	4.34	0.394	$1.85x10^{-2}$	69.6±1.4	30.1±3.0	67.3±1.4	99.7±4.4	97.4±4.4	4.40±0.33 (3)
	4.27	4.34	0.359	$9.78x10^{-2}$	87.8±3.2	10.0±4.0	90.7±2.5	97.8±7.2	101 ±6.5	8.52±0.23 (4)
Acetonitrile	7.96	7.62	1.00	-	77.2±1.0	17.5±1.6	73.9±1.6	94.7±2.6	91.4±5.2	1.12±0.04 (3)
	4.18	4.13	0.402	$4.27x10^{-2}$	84.4±3.6	17.5±3.2	85.3±1.9	102 ±6.8	103 ±5.1	4.85±0.23 (3)
	4.40	3.88	0.381	$9.09x10^{-2}$	92.2±0.2	8.0±1.0	92.3±0.7	100 ±1.2	100 ±0.3	8.74±0.05 (2)

a. Taken from ref. 128.
b. The reactions carried out with added Br_2 were run until 40-96% of the active halogen was used. Under these conditions the products reported did not vary more than the experimental limits listed. The remaining active halogen was always greater than $[Br_2]^o$.
c. RBr calculated as $[RBr + 2RBr_2 + CHCl_2Br$ (if done in CH_2Cl_2 solvent)].
d. (Moles of product/$[NBS]^o$-$[NBS]^f$) x 100.
e. The errors reported are average deviations from the mean value obtained. The numbers in parentheses are the number of independent experiments carried out.
f. Taken from Table XIII.

Table XV. The Effect of Added Olefin On The Relative Rates of Bromination of Cyclopentane (k_5) and Cyclohexane (k_6) With NBS (23°).

Solvent	Reactants, mol/lx10[1]				% Reaction[a]	Products, Yield (%)				Material Balance (%)[d]			k_5/k_6 [e]
	$[C_5H_{10}]$	$[C_6H_{12}]$	[NBS]	$[C_2H_4]$		RBr[b]	$C_2H_4Br_2$[c]	B-BPIC[d]	NSH	NS-	Br-	$CHCl_2Br$/B-BPIC	
Freon 113	7.15	9.80	0.498	-	76	100	-	-	-	-	100		9.94 [f]
	24.4	24.7	2.70	1.73	61	25.5	1.28	30.9	67.8	98.7	98.1		0.91
	24.4	24.7	2.81	1.59	63	24.0	1.20	36.1	62.1	98.2	99.5		0.88
Methylene Chloride	8.10	8.21	1.01	-	100	53.8±0.3	-	38.9±3.2	56.5±1.4	95.4±4.6	92.7±3.8	0.042	1.77±0.01(3)[i]
	24.7	24.1	2.99[g]	1.83	100	60.2	2.64	33.3 [h]	69.0	102.3	98.7	0.045	0.83
	8.09	7.46	0.998	0.658	100	53.7	3.26	(40.4) [h]	62.7	103.1	97.4	0.040	0.80
	8.02	8.00	0.964	0.292	100	56.9±0.6	3.45	(36.1±0.2) [h]	63.8±2.4	98.8±3.3	96.6±1.0	0.053	0.82±0.1(2)
Acetonitrile	7.96	7.62	1.00	-	100	73.9±1.6	-	17.5±1.6	77.2±1.0	94.7±2.6	91.4±5.2		1.12±0.04(3)[i]
	8.36	7.82	1.02	0.580	100	71.0	1.59	25.7	72.3	98.0	99.9		0.78
	8.36	7.82	1.02	0.722	100	80.5	1.57	16.4	83.7	99.9	100		0.78

a. Calculated as $([NBS]^o-[NBS]^f/[NBS]^o) \times 100$.
b. Calculated as $([RBr]/[NBS]^o-[NBS]^f) \times 100$; reactions in dichloromethane without ethylene include 1.6 ± 0.03% bromodichloromethane as one of the brominated materials used to calculate [RBr].
c. Calculated as $2([C_2H_4Br_2]/[NBS]^o-[NBS]^f) \times 100$.
d. ([Moles of product/$[NBS]^o-[NBS]^f$) x 100.
e. The errors reported are average deviations from the mean value obtained. The numbers in parentheses are the number of independent experiments carried out.
f. Taken from Table XIII.
g. The $[NBS]^o$ used somewhat exceeded its solubility at this temperature (0.20).
h. Values reported were obtained from the integrated 200-MHz ^1H NMR spectrum.
i. Taken from Table XIV.

The results in Table XIII show a dependence of k_5/k_6 upon the percentage conversion of NBS. This change might possibly indicate an increasing importance of reversal with hydrogen bromide (equation 42) as it was produced in the reaction. To measure the efficiency of hydrogen bromide trapping by NBS (equation 33) an isotope labelling experiment was run. Cyclohexane and perdeuteriocyclohexane were brominated with NBS in acetonitrile or dichloromethane. Mass spectral analysis of the alkane mixture before and after reaction showed no detectable incorporation of protium into the unbrominated deuteriocyclohexane or deuterium incorporation in the unbrominated cyclohexane. The same results were obtained with added bromine.

VI.2 Photobromination of Neopentane and Dichloromethane with NBS

The relative reactivity/H (r) of neopentane and dichloromethane to hydrogen abstraction by molecular bromine was determined and calculated using equation 50.

$$r = \left(k_{\text{neo}\,C_5H_{12}} \,/\, k_{CH_2Cl_2}\right) \Big/ H = \frac{\left[C_5H_{11}Br\right]}{\left[BrCHCl_2\right]} \cdot \frac{\left[CH_2Cl_2\right]^{\circ}}{\left[C_5H_{12}\right]^{\circ} \times 6} \qquad (50)$$

The conditions used and the results obtained are given in Table XVI. The reactions with bromine are qualitatively much slower than comparable reactions carried out with NBS, NBS/Br_2 or NBS/olefin mixtures. This behavior suggested the possibility that HBr reversal might be occurring since no HBr trap (eg. NBS) was present.

The reagent column of Table XVI contains numbers in parentheses which are the calculated ratio of Ave.[Br_2]/Ave.[HBr] (see footnote a, Table XVI). To obtain r values for bromine atoms uncomplicated by HBr reversal, low percentage conversions (<15%) were carried out to keep $([Br_2]/[HBr])_{ave.}$ large. The vapor phase brominations to low conversion, of substrates to products, using high concentrations of bromine relative to the substrate have been shown to yield relative reactivities in the absence of HBr or HBr_3 reversal.[128-132] The vapor phase r values obtained (r = 0.04) are very similar to the solution phase value reported,[119] r = 0.1. The solution phase r values obtained at low concentrations of bromine, 0.1-0.5 M (r = 0.05) are almost the same as those found for the vapor phase reactions. The solution phase r values obtained at high concentrations, 1-8 M, appeared to increase to 0.10 ± 0.02. The small increase in r may reflect a complexed radical (see 36) or a general solvation effect. The values obtained, however, are

Table XVI. The Competitive Photobromination of Neopentane and Dichloromethane with Molecular Bromine, 15°.

Reagent[a] $[Br_2]$	Substrates CH_2Cl_2/C_5H_{12}, mmol/mmol	Reaction (%)[f]	r[e]
NR[b]	NR/NR	3	0.1(1)
2.34×10^{4} (400/1)[c]	0.535/0.506	0.5	0.038
2.35×10^{-4} (400/1)[c]	0.550/0.571	0.5	0.038
2.75×10^{-3} (130/1)[d]	2.26 /2.24	1.5	0.035
5.42×10^{-1} (14/1)	31.2/4.54	8-15	0.047±0.004(3)
9.8×10^{-2} (15/1)	31.2/6.30	12.2	0.067
4.9×10^{-1} (53/1)	31.2/6.30	3.7	0.055
9.8×10^{-1} (77/1)	29.6/6.30	2.6	0.11
9.2×10^{-1} (370/1)	28.0/6.16	5.5	0.12
1.95 (250/1)	28.0/6.30	0.98	0.14
3.91 (420/1)	25.0/6.30	0.47	0.14
8.00	18.4/3.02	0.022	0.10
8.00	18.4/3.02	0.014	0.12
6.00	21.6/3.04	0.029	0.063
6.00	21.6/3.04	0.026	0.08
7.98	18.4/3.04	0.076	0.073
7.98	18.4/3.04	0.11	0.11

a. The values in parentheses are the average ratio of $([Br_2]^{\circ}+[Br_2]^{f})/[HBr]^{f}$.
b. NR - not reported. The r value reported is taken from reference 119.
c. Vapor phase reactions run in 12 ℓ reaction vessel at 23°.
d. Vapor phase reaction run in a 0.5 ℓ reaction vessel at 15°.
e. The errors reported are average deviations from the mean value obtained. The numbers in parentheses are the number of independent experiments carried out.
f. For the results, where $[Br_2]$ <6, the % reaction was determined by iodometric titration, while the remaining results were calculated on the basis of product yields.

$$Br-\dot{B}r-Br$$

36

identical to those previously reported.[119]

An experiment involving molecular bromine, hydrogen bromide, neopentane, and perdeuteriodichloromethane in carbon tetrachloride was carried out to demonstrate the importance of hydrogen bromide reversal. The initial ratio, $[Br_2]/[HBr] \equiv 1$, was designed to simulate the reaction conditions existing at 50% reaction. Mass spectral analysis of the dichloromethane before and after the reaction indicated an increase of 0.0101 M of protium. Since 0.0427 M of bromodichloromethane was shown to have been produced for the percentage reaction of bromine observed, one exchange occurred for every 4.23 bromination products produced. For the more energetic neopentyl radical a greater number of exchanges would be expected, although this is a minor product.

The substrates neopentane and dichloromethane were allowed to react with NBS (under homogeneous conditions) without any additives. Since the brominations of cyclohexane and cyclopentane under similar conditions showed changing relative reactivities with percentage conversion, a similar examination was undertaken with the unreactive substrates, neopentane and dichloromethane.

The conditions used and results obtained are presented in Table XVII.

At the lowest percentage conversion of NBS an r value = 1.89 was obtained. At 100% conversion the r value observed had decreased to 0.127 near the r value observed for molecular bromine (~0.05), and a 17% yield of β-BPIC had been produced.

Since the r values were observed to change with percentage reaction, the NBS bromination of neopentane and perdeuteriodichloromethane was carried out in order to determine whether the change was due to reversal with hydrogen bromide. Mass spectral analysis of the substrates before and after the reaction showed no increase of protium in the deuteriodichloromethane and no incorporation of deuterium into the unbrominated neopentane.

Neopentane and dichloromethane were brominated using NBS with added amounts of ethylene. The ratio [NBS]/[ethylene] was varied from ~9 to 620. When higher amounts of ethylene were used, [NBS]/[ethylene] ≅ 2, as in reference 119, only traces of $CHCl_2Br$ were found and substantial amounts of 1-bromo-3,3-dichloropropane were formed, and these results were discarded. If the ratio [NBS]/[ethylene] $\geq$ 9 was used none of the olefin addition product, 1-bromo-3,3-dichloropropane, was observed to be

Table XVII. The Competitive Photobromination of Neopentane and Dichloromethane with NBS, 15°.

Reagent	Substrates		Products, mol/mol of NBS°				Mass Balance, %		
[NBS]	CH_2Cl_2/C_5H_{12}, mmol/mmol	Reaction, %[a]	β-BPIC	NSH[b]	$CHCl_2Br$	$C_5H_{11}Br$	NS-	Br-	r
0.104	31.2/3.92	4.9	-[c]	0.034	0.0059	0.0084	98	97	1.89
0.104	31.2/3.92	13.3	0.042	0.088	0.015	0.016	100	94	1.44
0.104	31.2/3.92	18.3	0.059	0.17	0.038	0.029	105	95	1.03
0.104	31.2/3.92	23.6	0.096	0.13	0.046	0.033	99	94	0.965
0.104	31.2/3.96	33.1	0.079	0.20	0.12	0.046	95	91	0.517
0.104	31.2/3.92	39.8	0.13	0.19	0.17	0.056	93	96	0.432
0.104	31.2/3.90	49.8	0.13	0.32	0.22	0.046	96	90	0.276
0.104	31.2/3.90	81.6	-	-	0.45	0.065	-	-	0.193
0.104	31.2/3.92	97.1	0.17	0.74	0.71	0.074	94	99	0.138
0.104	31.2/3.90	100	0.17	0.73	0.81	0.077	90	105	0.127

a. Reaction percentage based on NBS consumed.
b. The product [NSH] was taken as the difference between the [NSH] after titration, and the [NBS] determined by titration after reaction.
c. (-) Signifies not measured.

formed. The conditions used and the results obtained are given in Table XVIII.

For reactions carried out with [NBS]/[ethylene] = 9 small amounts of brominated substrate (5-6%), and a large amount of β-BPIC (90-95%) were found to be formed. At low percentage conversion r = 22.9 was obtained, but was shown to decrease with percentage conversion of NBS. For reactions run at lower concentrations of ethylene, [NBS]/[ethylene] = 120, a high value r = 23.7 was obtained, at low percentage conversion of NBS, which decreased with percentage reaction. At the lowest concentration of ethylene employed, [NBS]/[ethylene] = 620, a value r = 5.25 was obtained, at low percentage conversion of NBS, which decreased with percentage reaction to a value r = 0.4. This low concentration of ethylene was equivalent to a 0.0086 molar % contamination of the neo-pentane with an olefin. The average high value of r = 19 ± 1.7 agrees well with the literature value (r = 21.3 ± 2.0[119] or 17[123]).

Photobrominations of neopentane and dichloromethane were carried out using NBS with added amounts of bromine. [NBS]/[Br_2] ratios from 125 to 5 were used to cover the range of conditions 0.5 to 100 reported[119] and to fit the limit, [Br_2] > 10^{-3} M, reported[122] to be conditions where no β-BPIC is produced. The results obtained and the

Table XVIII. The Competitive Photobromination of Neopentane and Dichloromethane with NBS-ethylene, 15°.

Reagent [NBS]/[C_2H_4]	Substrates CH_2Cl_2/C_5H_{12}, mmol/mmol	Reaction, %[a]	Products, mol/mol of NBS°					Mass Balance		r[c]
			β-BPIC	NSH[b]	$C_2H_4Br_2$	$CHCl_2Br$	$C_5H_{11}Br$	NS-	Br-	
2.0	8-300/1	NR[d]	0.5-0.7	NR	NR	NR	NR	NR	NR	21.3±2.0(2)[e]
$9.9x10^{-2}/1.1x10^{-2}$	31.2/0.38	80	0.71	0.051	0.024	0.024	0.032	96	102	17.8
$9.9x10^{-2}/1.1x10^{-2}$	31.2/0.38	82	0.71	0.067	0.027	0.028	0.038	95	100	18.3
$9.9x10^{-2}/1.1x10^{-2}$	31.2/0.38	77	0.71	0.024	0.025	0.024	0.031	96	104	17.9
$1.01x10^{-1}/1.13x10^{-2}$	31.2/0.38	11.3	0.056	0.014	0.012	0.0013	0.0021	96	97	22.9
$1.01x10^{-1}/1.13x10^{-2}$	31.2/0.38	32.1	-[f]	-	0.017	0.0071	0.0079	-	-	15.2
$1.01x10^{-1}/1.13x10^{-2}$	31.2/0.38	51.2	0.37	0.13	0.014	0.016	0.015	99	92	12.8
$1.01x10^{-1}/1.13x10^{-2}$	31.2/0.38	74.0	0.57	0.12	0.023	0.027	0.025	94	93	12.7
$1.02x10^{-1}/8.58x10^{-4}$	31.2/4.32	19.8	-	-	0.0021	0.0016	0.011	-	-	23.7
$1.02x10^{-1}/8.58x10^{-4}$	31.2/4.32	34.3	-	-	0.0045	0.0040	0.055	-	-	16.8
$1.02x10^{-1}/8.56x10^{-4}$	31.2/4.34	48.0	-	-	0.0066	0.0072	0.089	-	-	14.7
$1.02x10^{-1}/8.56x10^{-4}$	31.2/4.32	55.9	-	-	0.0072	0.014	0.096	-	-	8.45
$1.02x10^{-1}/8.56x10^{-4}$	31.2/4.38	55.9	-	-	0.0079	0.010	0.096	-	-	11.0
$1.02x10^{-1}/8.55x10^{-4}$	31.2/4.34	64.0	-	-	0.010	0.040	0.16	-	-	4.64
$1.02x10^{-1}/8.56x10^{-4}$	31.2/4.32	75.7	-	-	0.0085	0.071	0.16	-	-	2.68
$1.02x10^{-1}/8.57x10^{-4}$	31.2/4.32	86.5	-	-	0.0077	0.10	0.16	-	-	1.87
$1.02x10^{-1}/8.57x10^{-4}$	31.2/4.32	100	0.53	0.41	0.0095[g]	0.27	0.22	95	104	0.971
$1.04x10^{-1}/1.95x10^{-4}$	31.2/3.90	17.6	0.039	0.043	0.0018	0.0083	0.033	91	91	5.25
$1.04x10^{-1}/1.96x10^{-4}$	31.2/3.92	28.5	0.076	0.098	0.0029	0.020	0.054	89	87	3.68
$1.04x10^{-1}/1.87x10^{-4}$	31.2/3.90	37.1	-	-	0.0030	0.047	0.073	-	-	2.07
$1.04x10^{-1}/2.09x10^{-4}$	31.2/3.94	51.6	-	-	0.0032	0.070	0.081	-	-	1.52
$1.04x10^{-1}/2.05x10^{-4}$	31.2/3.88	56.9	0.22	0.36	0.0035	0.16	0.11	101	93	0.888
$1.04x10^{-1}/2.22x10^{-4}$	31.2/3.88	65.8	0.26	0.43	0.0024	0.27	0.093	103	96	0.469
$1.04x10^{-1}/2.32x10^{-4}$	31.2/3.88	88.7	-	-	0.0047	0.53	0.16	-	-	0.411
$1.04x10^{-1}/1.68x10^{-4}$	31.2/3.90	100	0.19	0.81	0.0057[g]	0.51	0.16	101	87	0.434

a. Reaction percentage based on NBS consumed.
b. The product [NSH] was taken as the difference between the [NSH] after titration, and the [NBS] determined by titration after reaction.
c. The errors reported are average deviations from the mean value obtained. The numbers in parentheses are the number of independent experiments carried out.
d. NR, not reported.
e. Values taken from reference 119.
f. (-) Signifies not measured.
g. The uncertainty in the measurement of [ethylene] may cause some of these yields to appear greater than possible.

conditions used are given in Table XIX.

Initial results obtained with this reagent, using Research grade neopentane[133] (Phillips Research grade, 99.97 or 99.92 mole %) and dichloromethane purified by distillation, gave erratic values of r ranging from 8-0.16 depending upon the amount of bromine added initially and its percentage reaction. It should be noted that the observed values of r were in the range reported with NBS/ethylene when the olefin added was only 0.0086 mole % of the neopentane present. The reaction solutions were also noted to decolorize before irradiation.

Using a number of other cylinders of neopentane (Phillips Research grade 99.97%) or by purification of the neopentane,[134] and using bromine freshly distilled over P_2O_5, only the relative reactivities reported in Table XIX could be obtained. The r values obtained were erratic and followed no pattern relative to the amount of bromine added. All of the r values, however, are less than the value reported[119] ($r = 1.15 \pm 0.16$) and averaged to $r = 0.20 \pm 0.13$. In all of the reactions carried out, measurable amounts of β-BPIC were formed.

Table XIX. The Competitive Photobromination of Neopentane and Dichloromethane with NBS-Br_2, 15°.

Reagent [NBS]/[Br_2]	Substrates CH_2Cl_2/C_5H_{12}, mmol/mmol	Reaction, %[a]	Products, mol/mol of NBS°				Mass Balance		$r^{c,d}$ (r)[e]
			β-BPIC[b]	NSH[b]	$CHCl_2Br$	$C_5H_{11}Br$	NS-	Br-	
(0.5-100/1)	(2-16/1)	14-96	0.00	NR[f]	NR	NR	NR	NR	1.15±0.16 (6)[g]
0.113/9.03x10^{-4}(125/1)	15.6/2.16	30.0	0.040	0.26	0.19	0.027	99	85	0.150 (0.171)
0.113/9.03x10^{-4}(125/1)	15.6/2.18	98.8	0.13	0.87	0.61	0.13	101	87	0.224 (0.254)
0.105/9.98x10^{-4}(105/1)	31.2/4.37	43.0	0.12	0.27	0.11	0.037	92	63	0.397 (0.400)
0.105/9.98x10^{-4}(105/1)	31.2/4.34	46.0	0.14	0.31	0.16	0.044	100	75	0.305 (0.329)
0.105/9.98x10^{-4}(105/1)	31.2/4.32	72.3	0.18	0.55	0.42	0.071	101	94	0.202 (0.201)
0.105/9.98x10^{-4}(105/1)	31.2/4.34	78.6	0.32	0.48	0.32	0.12	102	96	0.459 (0.449)
0.102/1.13x10^{-3}(90/1)	31.2/4.33	99.7	0.083	0.82	0.54	0.23	97	86	0.560 (0.512)
0.102/1.13x10^{-3}(90/1)	31.2/4.33	100	0.064	0.85	0.62	0.15	91	83	0.303 (0.290)
0.102/1.32x10^{-3}(78/1)	15.6/2.18	100	0.15	0.85	0.77	0.24	100	116	0.260 (0.372)
0.104/1.50x10^{-3}(69/1)	31.2/4.32	47.4	0.10	0.29	0.13	0.056	83	51	0.637 (0.525)
0.104/1.50x10^{-3}(69/1)	31.2/4.28	32.6	0.044	0.30	0.20	0.015	104	80	0.0894 (0.0911)
0.104/1.50x10^{-3}(69/1)	31.2/4.36	29.9	0.024	0.29	0.25	0.016	104	94	0.0750 (0.0763)

continued.....

Table XIX (continued):

$0.103/2.29x10^{-3}(45/1)$	31.2/4.32	92.2	0.078	0.92	0.79	0.092	108	104	0.170 (0.143)
$0.103/2.29x10^{-3}(45/1)$	31.2/4.32	94.7	0.079	0.92	0.88	0.095	105	111	0.151 (0.131)
$0.103/2.29x10^{-3}(45/1)$	31.2/4.32	96.6	0.073	0.93	0.78	0.084	104	97	0.161 (0.136)
$0.102/4.33x10^{-3}(24/1)$	31.2/4.33	54	0.031	0.45	0.36	0.037	88	79	0.124 (0.123)
$0.102/4.33x10^{-3}(24/1)$	31.2/4.33	63	0.045	0.59	0.44	0.087	101	90.8	0.215 (0.237
$0.101/4.15x10^{-3}(23/1)$	31.2/4.40	11-40	- [h]	-	-	-	-	-	0.0363±0.0009(5)[d]
$0.106/2.12x10^{-2}(5/1)$	31.2/4.34	76	0.037-	0.76-	0.59-	0.14-	104	101	0.288 (0.284)
$0.106/2.12x10^{-2}(5/1)$	31.2/4.34	96	0.039	0.99	0.85	0.15	107	108	0.216 (0.211)
$0.103/2.06x10^{-2}(5/1)$	31.2/4.33	98.8	0.031± 0.004	1.0± 0.09	0.90± 0.01	0.042± 0.001	105± 10	98.0± 0.9	0.0556±0.0004(2) (0.0560)

a. Reaction percentage based on NBS consumed.
b. The products, NSH and β-BPIC, were measured from the nmr spectra, relative to the unreacted NBS which was also determined by titration.
c. The errors reported are average deviations from the mean value obtained. The numbers in parentheses are the number of independent experiments carried out.
d. Products analyzed by Glpc.
e. Products analyzed by nmr.
f. NR, not reported.
g. Values taken from reference 119.
h. (-) Signifies not measured.

VI.3 Photoiodination of Neopentane and Dichloromethane with NIS/I_2

It had been reported[119-122] that reaction of neopentane and dichloromethane with NIS and added iodine gave r = 1.15 ± 0.12, and no observable production of β-iodopropionyl isocyanate (β-IPIC). The conditions used were 0.15 M NIS and 5×10^{-3} M I_2.[122] These results were a strong point in the argument that these conditions represented π-succinimidyl radical behavior.

Neopentane and dichloromethane were allowed to react with NIS in the presence of added iodine. The conditions used and the results obtained are presented in Table XX. The yield of succinimide is about twice the observed yield of iodinated substrates, RI, however unidentified signals in the nmr spectra amounted to <30% of the neopentyl iodide observed. The synthetic iodides were found to be unstable to light (freshly distilled materials rapidly developed a color characteristic of iodine upon exposure to room light) and the amounts detected were no doubt influenced by this fact. The r values obtained, 0.716 and 0.784, are smaller than, but similar to the reported values,[119,122] 1.15 and 1.08. The yields of β-IPIC were large, 75.0 and 72.6%, and do not agree with the report that no β-IPIC is formed.[119-122]

Table XX. The Competitive Photoiodination of Neopentane and Dichloromethane with NIS-I_2, 15°.

Reagent [NIS]/[I_2]	Substrates CH_2Cl_2/C_5H_{12}, mmol/mmol	Reaction, %[a] (Yield, %)	% Yield of Products[b] $CHCl_2I$[c]	$C_5H_{11}I$[c]	β-IPIC	NSH	r[d]
0.5-100/1[e]	2-16/1	NR[f] (1-6)	NR	NR	0	NR	1.15±0.12(4)
$0.15/5.0\times10^{-3}$[g]	125/4.00	NR (2.6)	2.17	0.450	0	NR	1.08
$0.046/4.6\times10^{-3}$(10/1)	15.6/2.22	51-90 (12.4)	7.66±0.34	4.69±0.11	75.0±3.4	25.1±3.4	0.716±0.016(2)
$0.051/2.2\times10^{-3}$(23/1)	15.6/2.16	61-79 (12.3)	7.46±1.65	4.84±0.76	72.6±2.5	27.4±2.5	0.784±0.046(3)

a. Reaction percentage and percentage yield of products based on NIS consumed.
b. Determined by integrations obtained from the 200 MHz ^1H nmr.
c. Determined by Glpc and nmr.
d. The errors reported are average deviations from the mean value obtained. The numbers in parentheses are the number of independent experiments carried out.
e. Taken from reference 119.
f. NR, not reported.
g. Taken from reference 122.

VI.4 The Graded Series

Because of the experimental discrepancies observed by Walling,[125] and those obtained in this laboratory, it was felt to be worthwhile reinvestigating the results presented in the graded series.[123] The reported experimental recipe for these reactions was given as 1.69 mmol of NBS in 78 mmol (5 ml) of dichloromethane. When this recipe was followed, in this laboratory the mixture was found to be heterogeneous, with 50% to 90% of the NBS insoluble (determined by titration of the filtered solution with aqueous thiosulfate).

Experiments from the graded series,[123] chosen to cover the range of substrates reported, were carried out using the experimental recipe given. Reaction mixtures were run to 100% conversion of NBS as determined by titration with standardized sodium thiosulfate solution. The conditions used and the results obtained are presented in Table XXI.

Excluding the results obtained in the presence of benzene, and in solvent chloroform the ratios $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained for each added substrate vary unpredictably, but not significantly. The average ratio $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained for these experiments is 0.046 ± 0.017. The value obtained with added benzene

Table XXI. The Photobromination of a Graded Series of Substrates with NBS-vinylidene chloride[a] in Dichloromethane, 15°.

Substrates (M)[b]	Products (mmol)	$\frac{[BrCHCl_2]}{[\beta\text{-BPIC}]}$	$\frac{[BrCHCl_2]^c}{[\beta\text{-BPIC}]}$	Exp.[c] No.
CH_2Cl_2 (15.6) CH_2CCl_2 (0.071)	β-BPIC (0.54±0.02) $BrCHCl_2$ (0.042±0.008) succinimide (0.13±0.007) $BrCH_2CCl_2Br$ (0.0090±0.0004)	0.078±0.020	0.024	1
CH_2Cl_2 (15.3)[d] neo-C_5H_{12} (0.19) C_2H_4 (0.011)	β-BPIC (0.14) $BrCHCl_2$ (0.0050±0.0004) $C_5H_{11}Br$ (0.0067±0.0006) succinimide (0.0094±0.0031) $BrCH_2CH_2Br$ (0.0050±0.0002)	0.026±0.003	0.021	2
CH_2Cl_2(13.1)[e] cyclopentane (0.80) cyclohexane (0.80) C_2H_4 (0.030)	β-BPIC (0.070±0.0001) $BrCHCl_2$ ($0.0037\pm2\times10^{-5}$) C_5H_9Br (0.048±0.001) $C_6H_{11}Br$ (0.058±0.0005) succinimide (0.12±0.008) $BrCH_2CH_2Br$ ($0.0036\pm6\times10^{-5}$)	0.063±0.004	0.025	7
CH_2Cl_2 (14.9) 2,3-dimethylbutane (0.41) CH_2CCl_2 (0.073)	β-BPIC (0.30±0.002) $BrCHCl_2$ (0.014±0.0008) 1-bromo-C_6H_{13} ($0.0068\pm2\times10^{-5}$) 2-bromo-C_6H_{13} (0.011±0.0003) succinimide (0.39±0.006) $BrCH_2CCl_2Br$ (0.044±0.001)	0.041±0.001	0.045	9
CH_2Cl_2 (15.0) cyclohexene (0.38) CH_2CCl_2 (0.085)	β-BPIC (0.036±0.016) $BrCHCl_2$ ($(7.6\pm0.3)\times10^{-4}$) 4-bromo-C_6H_9 (0.0048±0.0001) 3-bromo-C_6H_9 (0.019±0.005) 1-bromo-2-succinimidyl-C_6H_{10} (0.15±0.01) succinimide (0.39±0.004) 1,2-dibromo-C_6H_{10} (0.19±0.02) 1,3-cyclohexadiene (0.020±0.007) benzene (0.010±0.0008)	0.023±0.034	0.073	10

continued.....

Table XXI (continued):

CH_2Cl_2 (15.0) benzene (0.40) CH_2CCl_2 (0.085)	β-BPIC (0.16±0.002) $BrCHCl_2$ (0.11±0.015) N-phenylsuccinimide (0.051±0.003) succinimide (0.38±0.054) $BrCH_2CCl_2Br$ ($0.015±4x10^{-4}$) 6-succinimidyl-3,4,5-tribromocyclohexene (0.046±0.011)	0.685±0.087	0.294	12
CH_2Cl_2 (15.0) 1,3-butadiene (0.36) CH_2CCl_2 (0.073)	β-BPIC ($0.15±5x10^{-4}$) $BrCHCl_2$ ($0.0063±2x10^{-4}$) NS-CH_2CH=CHCH_2Br, NS-CH_2CHBrCH=CH_2 (0.51±0.002) Br-CH_2-CH=CH-CH_2Br ($0.08±5x10^{-4}$)	$0.043±6x10^{-5}$	>0.322	-
$CHCl_3$ (12.4)[g] CH_2CCl_2 (0.06)	β-BPIC (0.16±0.003) $BrCCl_3$ ($(8.6±1.2)x10^{-4}$) succinimide (0.033±0.003) $BrCH_2CCl_2Br$ ($(4.5±0.6)x10^{-4}$)	0.0051±0.0042	>5.0[f]	18

a. Vinylidene chloride (1,1-dichloroethylene) was the olefin used unless stated otherwise.
b. Reaction conditions taken from reference 123 unless stated otherwise (0.68 mmol of NBS in 2 ml of CH_2Cl_2).
c. Results taken from Table XII.
d. Results taken from Table XVIII.
e. Results taken from Table XV.
f. $[BrCCl_3]/[\beta\text{-BPIC}]$.
g. 0.20 mmol of NBS in 2 ml of $CHCl_3$

(exp. no. 12, Table XXI) is larger than, but similar to the value reported,[123] and significantly larger than the average value obtained upon addition of the other substrates. The value obtained with chloroform is much smaller than the value reported[123] and likewise, smaller than the average value.

Two other results differ significantly from the reported results. The 200 MHz ^{1}H nmr spectrum for the product mixture obtained with cyclohexene showed a singlet near the expected shift for bromodichloromethane. Addition of authentic bromodichloromethane however, produced a new nmr signal showing it to be some other product, see Figure 3 (a similar result was obtained by Glpc analysis, see Figure 4). A Glpc-mass spectrum indicated it to be benzene. The assignment was confirmed by the addition of benzene to the sample and repeating the nmr and Glpc analyses. The Glpc analysis also indicated the presence of 1,3-cyclohexadiene and traces of bromodichloromethane.

Since Glpc analysis of the cyclohexene used showed the presence of traces of benzene and 1,3-cyclohexadiene, an experiment designed to determine whether benzene was produced in the reaction was carried out. Reaction mixtures were prepared in nmr tubes in the same manner as was the experiment run with added cyclohexene. An nmr

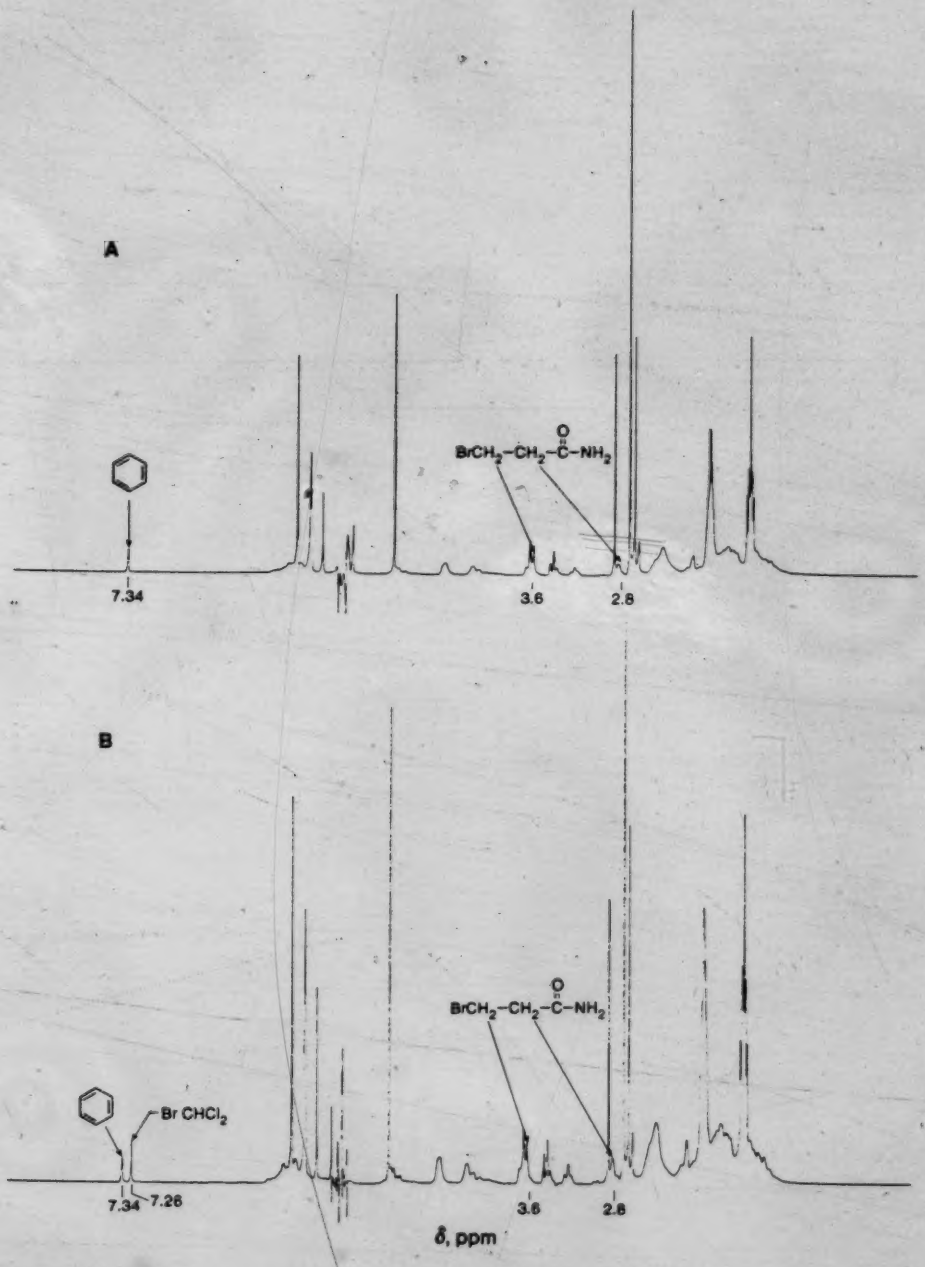


Figure 3. A. 200 MHz ^{1}H NMR Spectrum of the Reaction Product Mixture from the Photobromination of Dichloromethane with NBS-vinylidene Chloride with Added Cyclohexene.
B. Results of A after the Addition of 6×10^{-5} moles of Bromodichloromethane.

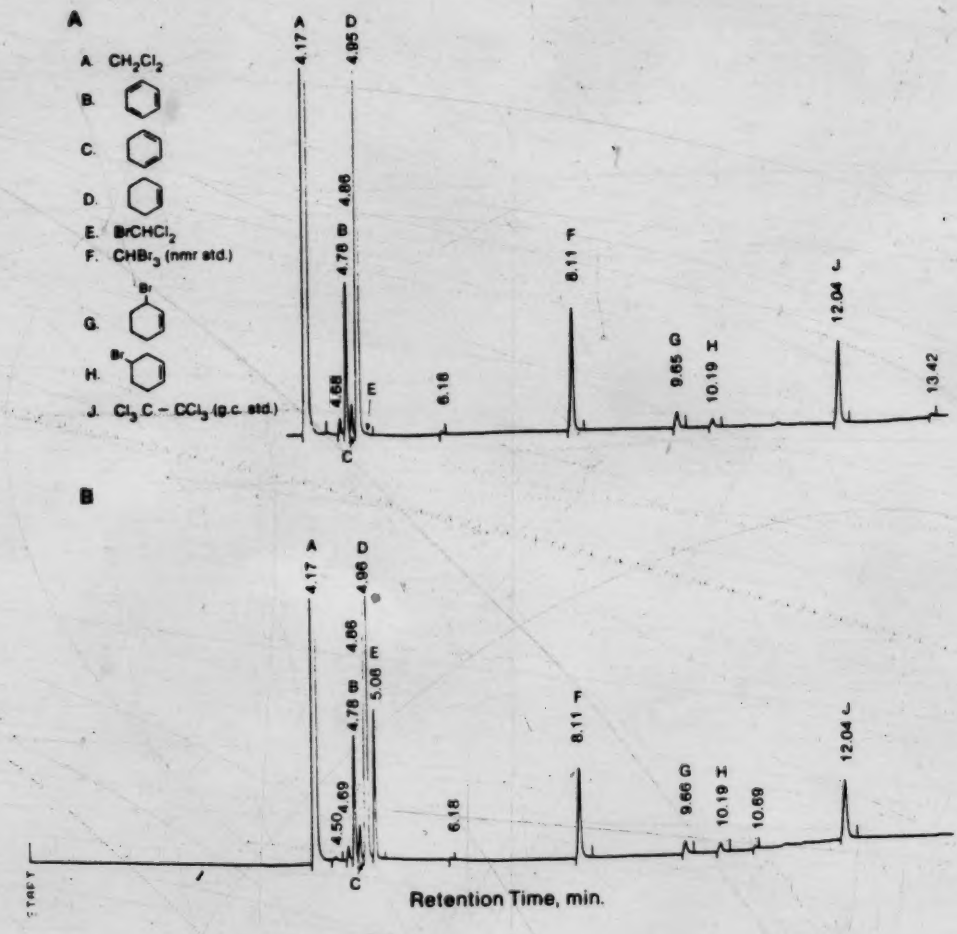


Figure 4. A. Capillary Gas Chromatogram of the Reaction Product Mixture from the Photobromination of Dichloromethane with NBS-vinylidene Chloride with Added Cyclohexene.
B. Results of A after the Addition of 6×10^{-5} moles of Bromodichloromethane.

spectrum before irradiation showed a barely measurable benzene singlet which was measured relative to bromoform as an added internal standard. After irradiation an nmr spectrum showed a large benzene singlet and no singlet for bromodichloromethane. Measurement relative to bromoform indicated the production of 5.25×10^{-6} moles of benzene (1.5% yield based on NBS used). Addition of bromodichloromethane produced a new signal (δ7.26) and addition of benzene verified the assignment of the nmr signal to benzene.

The result obtained with 1,3-butadiene also differed from the reported results. The 200 MHz ^1H nmr spectrum for the product mixture obtained showed a pair of singlets near the expected shift for bromodichloromethane, but no signal for bromodichloromethane was observed (demonstrated by addition to the sample of authentic bromodichloromethane), see Figure 5. To determine the identity of the observed pair of singlets the reaction was run again, however since the original cylinder of 1,3-butadiene had been exhausted a new cylinder was used. This experiment produced an nmr spectrum lacking the observed singlets and no measurable signal for bromodichloromethane, see Figure 6 (Glpc analysis showed traces of bromodichloromethane). Since the original cylinder was nearly empty when used, and a

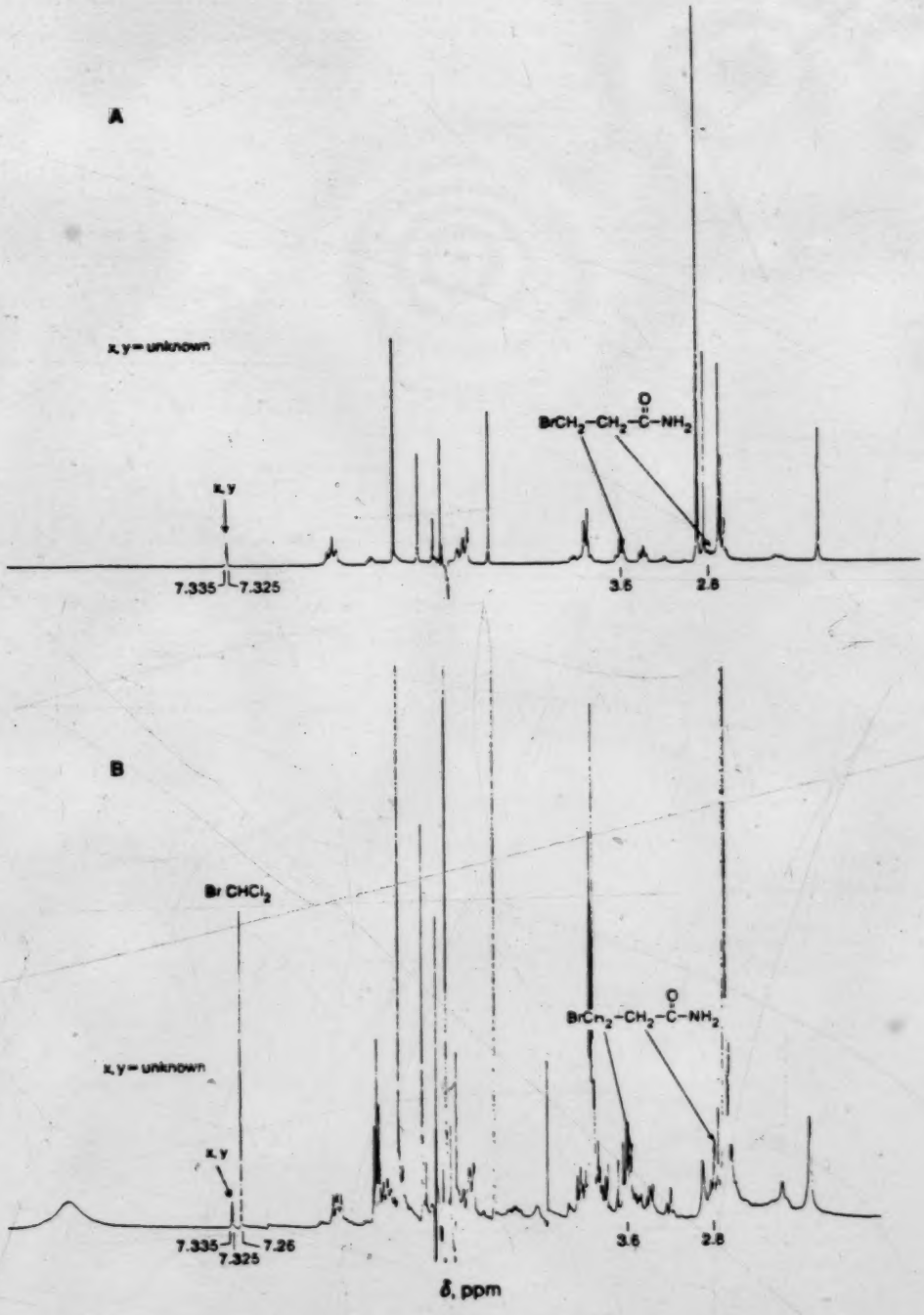


Figure 5. A. 200 MHz ^{1}H NMR Spectrum of the Reaction Product Mixture from the Photobromination of Dichloromethane with NBS-vinylidene Chloride with Added 1,3-Butadiene.
B. Results of A after the Addition of 6.9×10^{-5} moles of Bromodichloromethane.

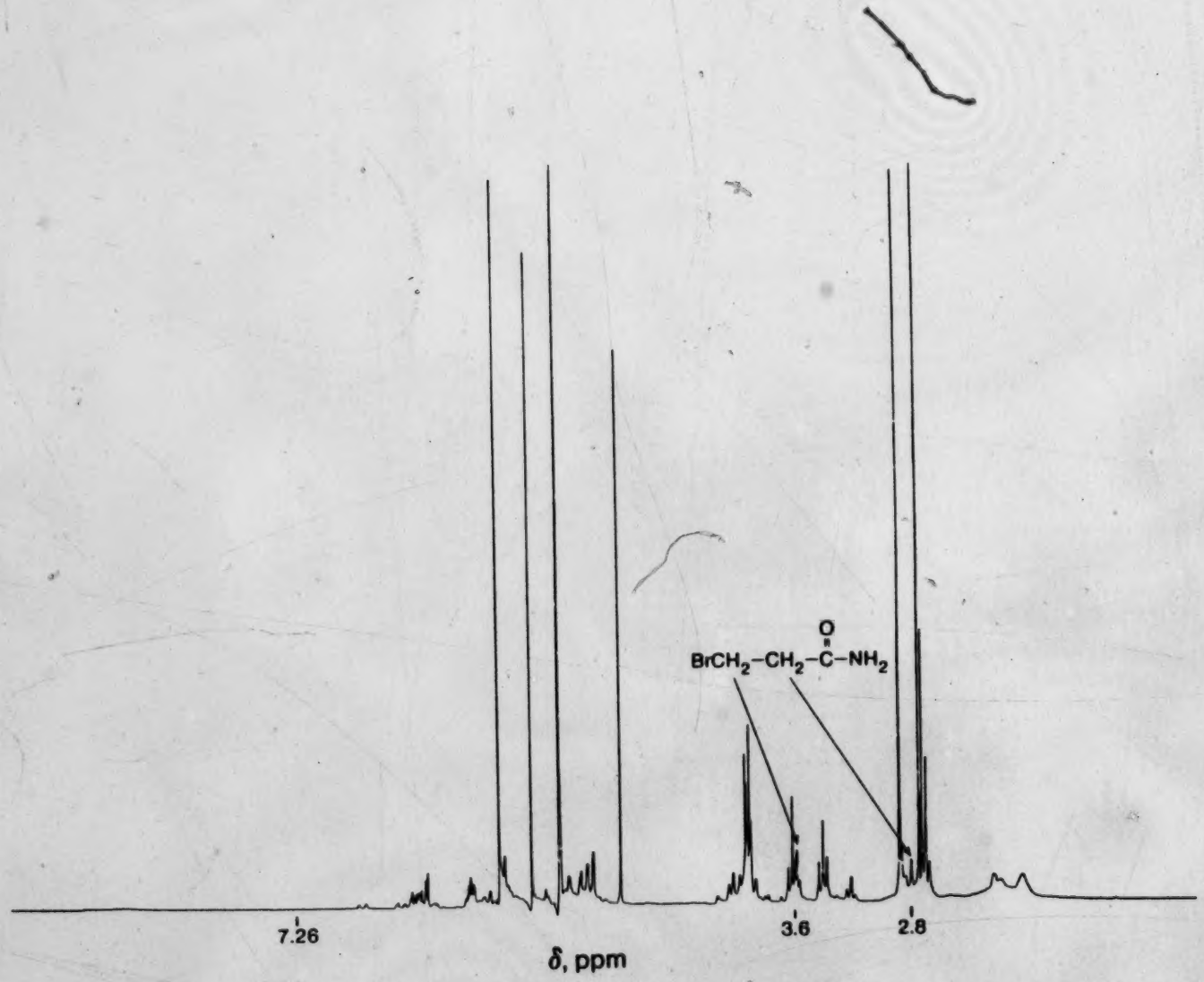


Figure 6. 200 MHz ^{1}H NMR Spectrum of the Reaction Product Mixture from the Photobromination of Dichloromethane with NBS-vinylidene Chloride with Added 1,3-Butadiene (New Cylinder).

fresh cylinder failed to yield the unidentified signals, they were assumed to be impurities present in the original cylinder of 1,3-butadiene.

VI.5 Photobromination of Dichloromethane with NBS-olefin in the Presence of Benzene

During the experiments with benzene presented in Table XXI (exp. no. 12) it was noted that the results were not reproducible and might be dependent upon the percentage conversion of the NBS.[135] To investigate this further, experiments number 11 and 13 from Table XII were repeated, and carried out to various degrees of NBS conversion. The conditions used and the results obtained are given in Table XXII. The ratios $[BrCHCl_2]/[\beta\text{-BPIC}]$ were observed to be dependent upon percentage conversion of NBS, going from low values at low percentage reaction to higher values at high percentage reaction. This result suggested that more than one abstracting species was involved in producing the ratios observed.

Since, from the results obtained with cyclopentane and cyclohexane, it was apparent that NBS under insoluble conditions (i.e. in benzene, Freon 113 or carbon tetrachloride) gave different results than when run under soluble conditions, and since the NBS in these experi-

Table XXII. The Photobromination of Dichloromethane with NBS-vinylidene Chloride in the Presence of Benzene, 15°.

Reagent, M[a] [NBS]/[CH_2CCl_2]	Substrates, M [CH_2Cl_2]/[C_6H_6]	Reaction, %[b]	[$BrCHCl_2$] / [β-BPIC]	[$BrCHCl_2$][c] / [β-BPIC] (Reaction, %)
0.34/0.080[d]	15.3/0.20	48.7	0.164	0.138 (69.2)
0.34/0.074[d]	15.3/0.20	54.2	0.249	
0.34/0.074[d]	15.3/0.20	58.9	0.298	
0.34/0.080[d]	15.3/0.20	73.7	0.889	
0.34/0.074[d]	15.3/0.20	97.1	1.653	
0.34/0.15	15.3/0.20	40.0	0.239	
0.34/0.14	15.3/0.20	55.2	0.110	
0.34/0.14	15.3/0.20	60.5	0.103	
0.34/0.15	15.3/0.20	73.4	0.245	
0.34/0.15	15.3/0.20	87.4	0.694	
0.34/0.072[d]	14.5/0.78	30.8	0.177	0.609 (39.6)
0.34/0.072[d]	14.5/0.78	45.2	0.980	
0.34/0.072[d]	14.5/0.78	52.7	1.631	
0.34/0.072[d]	14.5/0.78	67.4	1.270	
0.34/0.072[d]	14.5/0.78	83.3	2.180	
0.34/0.15	14.5/0.78	48.1	0.200	
0.34/0.15	14.5/0.78	54.1	0.256	
0.34/0.15	14.5/0.78	60.7	0.366	
0.34/0.15	14.5/0.78	67.1	0.511	

a. The [NBS] shown is what would exist if the NBS were soluble. The solution is heterogeneous.
b. Based upon the amount of NBS consumed.
c. Taken from Table XII and reference 123.
d. Reaction conditions used are those presented in ref. 123.

ments was largely insoluble, this was considered to be an important factor in the observations. It had been proposed[110] that when NBS was insoluble, but bromine was soluble, the reaction is dominated by a bromine atom chain. It was therefore considered important to check for the presence of a competing bromine atom chain in these experiments.

The same two conditions (exp. 11 and 13, Table XII) were repeated with twice as much olefin and carried out to various degrees of NBS conversion. These results are also presented in Table XXII. Changing values of the ratio $[BrCHCl_2]/[\beta\text{-BPIC}]$ were once again observed, however the values obtained were roughly half as large as were obtained with the lower amount of olefin. The results do not always show a smooth change in reactivity and sometimes a value cannot be obtained from the preceeding value. It should be noted however, that these are all independent reaction mixtures and this variability is probably due to differences in amounts of inhibitors present and the intensity of the light used to initiate the reaction.

VI.6 Photobromination of Chloroform with NBS

The bromination of chloroform with NBS (Table XXI, exp. 18) yielded a result differing greatly from the

previous report,[123] but similar to that obtained when dichloromethane was brominated with NBS (Table XXI, exp. 1). Because of this observed similarity in reactivity for dichloromethane and chloroform it was considered worthwhile to compare the reactivities with the two substrates. The conditions used and the results obtained are given in Table XXIII.

When NBS was photolyzed in chloroform without any additives large yields of bromotrichloromethane (85.5%) and succinimide (80.2%) were produced with a moderate yield (19.8%) of β-BPIC being formed. This compares well with the reaction of the substrates neopentane and dichloromethane with NBS without additives, where a yield of 88.7% of brominated substrates and a 17% yield of β-BPIC was produced (see Table XVII).

When NBS and added bromine were allowed to react with chloroform, bromotrichloromethane and succinimide were produced almost quantitatively, with only a small amount of β-BPIC, 2.31%, being produced. The analogous reaction of NBS and added bromine with neopentane and dichloromethane as substrates likewise showed high yields of brominated substrates (85-100%), with yields of β-BPIC between 3.7 and 15% (see Table XIX).

Bromination of chloroform with NBS and added vinylidene chloride gave very small yields of bromotrichloro-

Table XXIII. The Photobromination of Chloroform with NBS and Additives, 15°.

Reagent, M		Substrate, M		Yield of Products, %[a,b]				Mass Balance, %	
Additive	[NBS]	[Additive]	[$CHCl_3$]	Reaction, %[a]	CCl_3Br	C_2Cl_6	β-BPIC	NSH	NS-	Br-
None	0.099	-	12.4	100	85.5	0	19.8	80.2	100	105
Bromine	0.096	0.0011	12.4	100	101	0	2.31	97.7	100	103
Vinylidene Chloride	0.096	0.063	12.4	100	1.38±1.0	0	82.7±1.5	17.4±1.4	100	84.1±0.4
Vinylidene[c] Chloride	0.34	0.08	12.4	35.5	100	0	0	100	100	100
Vinylidene[d] Chloride	0.11-0.13	0.088-0.052	12.4	100-78	N.R.	N.R.	81-79	N.R.		

a. Based on the amount of NBS consumed.
b. The errors reported are the average deviation from the mean value obtained.
c. Results taken from reference 123.
d. Results taken from reference 125.

methane (1.38%) and succinimide (17.4%) and a large yield of β-BPIC, 82.7%. This result agrees with the results obtained with NBS and added ethylene with neopentane and dichloromethane, where low yields of brominated substrate were formed (~7%) and the yield of β-BPIC was 89-95% (see Table XVIII). This result however does not agree with the original report of 0% yield of β-BPIC,[123] but is in good agreement with results reported later by Walling.[125]

Chloroform was added to a reaction of NBS-ethylene with neopentane and dichloromethane. The concentrations of chloroform and dichloromethane were roughly equal and yields of brominated product obtained from the two solvents were roughly equivalent. The added chloroform produced no noticeable change in the r values obtained. The values obtained, r = 17.6-9.69, for 25-60 percent conversion are in good agreement with the values obtained in the absence of chloroform (see Table XVIII). A full description of the results obtained is given in Appendix II.

Addition of chloroform to a reaction of NBS-bromine with neopentane and dichloromethane was also carried out. Again the concentrations of chloroform and dichloromethane were roughly equal and the yield of brominated product was actually greater from chloroform

than from dichloromethane. The values of r obtained, 0.086 and 0.048, for 18 and 100 percent conversion are similar to those obtained in the absence of chloroform (see Table XIX). A full description of the results obtained is given in Appendix II.

It had been reported[125] that some of the β-BPIC formed in chloroform was photochemical in origin. Since this report also claimed no β-BPIC was formed with NBS in chloroform without additives, and a yield of 19.8% was observed here, it was considered to be important to determine the amount of β-BPIC which would be formed under thermal initiation only. Chloroform was allowed to react with NBS and either di-tert-butylperoxyoxalate (DBPO) or AIBN at temperatures between 15 and 60°C in the dark. The results obtained are given in Table XXIV. At 15°C the yield of β-BPIC was about half that obtained in the photoinitiated reactions. The yield of β-BPIC was observed to increase with increasing temperature.

VI.7 Photoiodination of Chloroform with NIS and Iodine

Since large yields of β-IPIC were observed for the photoiodination of neopentane and dichloromethane with NIS and iodine, the iodination of chloroform with NIS and

Table XXIV. The Thermally Initiated Reaction of NBS with Chloroform in the Dark.

Reagent, M			Substrate, M			
Initiator	[NBS]	[Initiator]	[$CHCl_3$]	Temperature, °C	Reaction, %[a]	Yield β-BPIC, %[a,b]
DBPO[c]	0.074	0.0052	12.4	15	49-63	10.5±2.7
DBPO	0.074	0.0050	12.4	22.5	61-65	27.8±0.9
DBPO	0.074	0.0050	12.4	40	81-84	29.5±2.6
AIBN[d]	0.082	0.0075	12.4	60	60	59.8±3.8

a. Based on the amount of NBS consumed.
b. The errors reported are the average deviation from the mean value obtained.
c. DBPO, di-tert-butylperoxyoxalate.
d. AIBN, α,α'-azobisisobutyronitrile.

iodine was investigated. The conditions used and the results obtained are presented in Table XXV. Large yields of β-IPIC, 69.2-75.3%, were obtained with only small amounts of iodinated substrate and succinimide being formed. The yields of β-IPIC formed in these reactions were comparable to those obtained in the iodination reactions of neopentane and dichloromethane (72.6-75.0%, see Table XX) with this reagent.

Table XXV. The Photoiodination of Chloroform with NIS-I_2, 15°.

Reagent, M	Substrate, M		Yield of Products, %[a]			
[NIS]/[I_2]	[$CHCl_3$]	Reaction, %[a]	CCl_3I	C_2Cl_6	β-IPIC	NSH
0.017/0.011 (1.5/1)	12.4	100	2.63	0.218	75.3	24.7
0.024/0.0026 (9.2/1)	12.4	100	1.37	0.232	69.2	30.8

a. Based on the amount of NIS consumed.

DISCUSSION

The investigations outlined in the introduction do not provide a clear description of the effects of solvent choice, concentration of the reagent, the additives used (olefin or molecular bromine) and substrate reactivity upon the nature of the abstracting radical observed to be present (NS· or Br·) in the NBS photobrominations. Competitive photobromination of two substrates, which do not contain polar groups (cyclopentane and cyclohexane), using NBS was chosen to illustrate the importance of solvent choice and additives used to moderate the reaction.

The question of the abstracting species is further complicated by the proposal[119-124] that two thermally accessible states of succinimidyl radical (π or σ) can exist in solution. This proposal was based upon evidence that the relative reactivity of neopentane and dichloromethane to the NBS containing reagents differentiates between the π- (r = 1.15) and σ- (r = 21.3 or 17) radicals, that the same radical (π-NS·) is formed using the NIS-I_2 reagent as with the NBS-Br_2 reagent, and that the production of the ring opened product (β-BPIC) arises cleanly from the σ- and not the π-radical. Based on the rationalization of this evidence, a kinetic argument was

also proposed[123] to identify the succinimidyl radical present (π or σ) in the reactions of NBS with a series of added substrates. The ratio of $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained was suggested to be a measure of the relative importance of the π- and σ-succinimidyl radicals in the presence of substrates with varying reactivities.

VII.1 Reactions of NBS with Cyclohexane and Cyclopentane

The results obtained from the photobromination of cyclohexane and cyclopentane, using the NBS containing reagents, provide a clear description of the effects of solvent choice and additives used (olefin or molecular bromine) to moderate the reaction, upon the reactivities obtained. The effect of the solvent choice on the relative rates of bromination of cyclohexane and cyclopentane can be seen in Table XIII. The solvents can be divided into two categories; one in which cyclopentane is brominated 9-10 times faster than cyclohexane, and one in which the two hydrocarbons are brominated at nearly the same rate. The solvents can also be divided into two categories based on NBS solubility; one in which NBS is soluble, and one in which NBS is insoluble. These two classifications coincide, such that in the solvents in which NBS is insoluble or only slightly soluble (Freon

113 and benzene) cyclopentane is brominated 9-10 times faster than cyclohexane, and in the solvents in which NBS is soluble (dichloromethane and acetonitrile) the two hydrocarbons are brominated at nearly the same rate. The higher of the two relative reactivity ratios obtained is nearly identical to the ratio reported for the bromination rates of the two hydrocarbons with molecular bromine, in the absence of hydrogen bromide reversal (see the first two entries of Table XIV).

The lower relative reactivity ($k_5/k_6 = 0.8$) obtained for the brominations in acetonitrile is attributed, by elimination, to a less selective succinimidyl radical chain. The dependence of the relative reactivities upon solvent can be explained in an analogous manner to that presented in a communication concerning the mechanism of allylic bromination.[110] Because it is highly soluble in dichloromethane and acetonitrile, the concentration of NBS remains high in these solvents, and the succinimidyl chain remains dominant. In the solvents where the NBS is insoluble only the bromine atom chain proceeds, since radical transfer with the solid NBS is slow. The previous report[110] suggested that the succinimidyl chain proceeded only in the presence of olefinic materials, and the bromine atom chain quickly takes over the propagation sequence in the absence of olefins. This appears to be

contradictory to other reports,[109] and the results presented in Table XIII, for experiments carried out in dichloromethane or acetonitrile, although the relative reactivities do change somewhat with percentage conversion of NBS. The changeover from a succinimidyl radical to a bromine atom chain is no doubt dependent upon the ease of reaction of the substrates in question with the two chain-carrying radicals.

The observation that isotope exchange between cyclohexane and perdeuteriocyclohexane did not occur in the presence of NBS can rule out the hydrogen bromide reversal step (equation 42) as a factor that contributes to the dependence of the relative rate ratio upon the percentage reaction observed in Table XIII. The alternative explanation therefore, is that the bromination can proceed by a mixed chain. As the percentage conversion of NBS decreases its concentration, the rate of its transfer with an alkyl radical becomes slower, and the concentration of generated succinimidyl radicals decreases. Bromine atoms, generated from the small amounts of bromine which form during the reaction, begin to compete with succinimidyl radicals for abstraction from the substrates, and the reaction is increasingly dominated by the bromine atom chain. As the concentration of bromine increases the importance of the succin-

imidyl radical chain may be further lessened by a transfer reaction between the NS· radical and molecular bromine (equation 51).

$$NS\cdot + Br_2 \longrightarrow NBS + Br\cdot \qquad (51)$$

The relative rates obtained when ethylene was added to the reaction mixture were all lower than the ratios obtained without additives. The lower values (see Table XV) represent the selectivity of the succinimidyl radical. In the reaction carried out in a solvent which favors the bromine atom chain (Freon 113), the addition of ethylene appears to completely suppress the bromine atom chain, such that the succinimidyl radical chain dominates the propagation sequence. In the solvents which favor the succinimidyl radical chain (dichloromethane and acetonitrile), the addition of ethylene suppresses the small contribution of the competing bromine atom chain, and the relative reactivity observed (k_5/k_6 = 0.8) is that of the succinimidyl radical.

The relative rate ratios obtained when bromine was added to the reaction mixture (see Table XIV) were all higher than the ratios obtained without additives. The addition of small amounts of bromine ensured the dominance of the bromine atom chain in the solvents which

favor it (Freon 113 and benzene). The bromine atom chain could also be made to dominate in solvents which favored propagation by succinimidyl radicals (dichloromethane and acetonitrile) if sufficient bromine was added.

None of the results obtained suggested the involvement of a third abstracting radical species. The suggestion that for the NBS-bromine experiments, with bromine concentrations $>10^{-3}$ M, a π-succinimidyl radical is the abstracting species[122] was based on the argument that no β-BPIC is formed under these conditions. Table XIV clearly demonstrates that, at least for cyclohexane and cyclopentane, this statement is not true since appreciable yields of β-BPIC (8-30%) were obtained under these conditions. Table XV shows that with or without added ethylene the ratio $[BrCHCl_2]/[\beta\text{-BPIC}]$ is the same (within experimental error). It is therefore concluded that with the NBS-Br_2 reagent, the bromine atom chain dominates, while with the NBS-olefin reagent, the succinimidyl radical is the dominant chain-carrying species, and presumably in all solvents it is the ground state radical.

VII.2 Reactions of Neopentane and Dichloromethane with NBS and NIS.

Although the results obtained with cyclopentane and

cyclohexane do not demand two states of the succinimidyl radical, they also do not invalidate the proposal that the two states are present. A detailed investigation of the results obtained with the substrates, neopentane and dichloromethane, yielded further insights into this question.

The relative reactivity, r, was seen to change during the course of the bromination of neopentane and dichloromethane with NBS. At low conversion r (1.89) was between the value found with NBS-ethylene and that for the reactions of these substrates with molecular bromine. At completion of the reaction r (0.127) approached that found for molecular bromine (~0.05) in the absence of reversal (see Table XVI).

Since reversible abstraction was shown not to take place during NBS brominations, the change in reactivity can be attributed to the competition of two abstracting chains whose relative contributions change with percentage conversion of NBS. The average relative reactivity obtained using the high concentration of ethylene, r = 19, represents the value attributable to the succinimidyl radical. The addition of ethylene serves to suppress the competing bromine atom chain by lowering the molecular bromine concentration in solution. The addition of molecular bromine to the reaction

mixture causes the bromine atom chain to dominate the propagation sequence giving, at the highest [Br_2], r values (0.056) similar to those obtained with molecular bromine in the absence of hydrogen bromide reversal (0.05).

The detection of appreciable amounts of β-BPIC in all of the NBS reaction mixtures studied (with or without additives) is contrary to the reported results[119-122] (see Figure 7). It was not possible to reproduce the reported r value (1.15)[119] for NBS-bromine. NBS-ethylene mixtures or reactions of NBS alone which passed through this value of r all showed significant yields of β-BPIC. It therefore appears that the same succinimidyl radical (presumably the ground state) must be present no matter which reaction conditions are used.

The failure of previous reports[119-122,125] to observe β-BPIC in the NBS-Br_2 reactions can be explained by two considerations. Both[119-122,125] groups who reported these reactions previously, relied heavily upon infrared detection of the product isocyanate. In reactions run in this laboratory, nmr analysis always showed mixtures of isocyanate and β-bromopropionamide (β-BPA). Since it was determined that milligram quantities of water, or less, were required to quantitatively convert the β-BPIC to β-BPA, the limitations of infrared

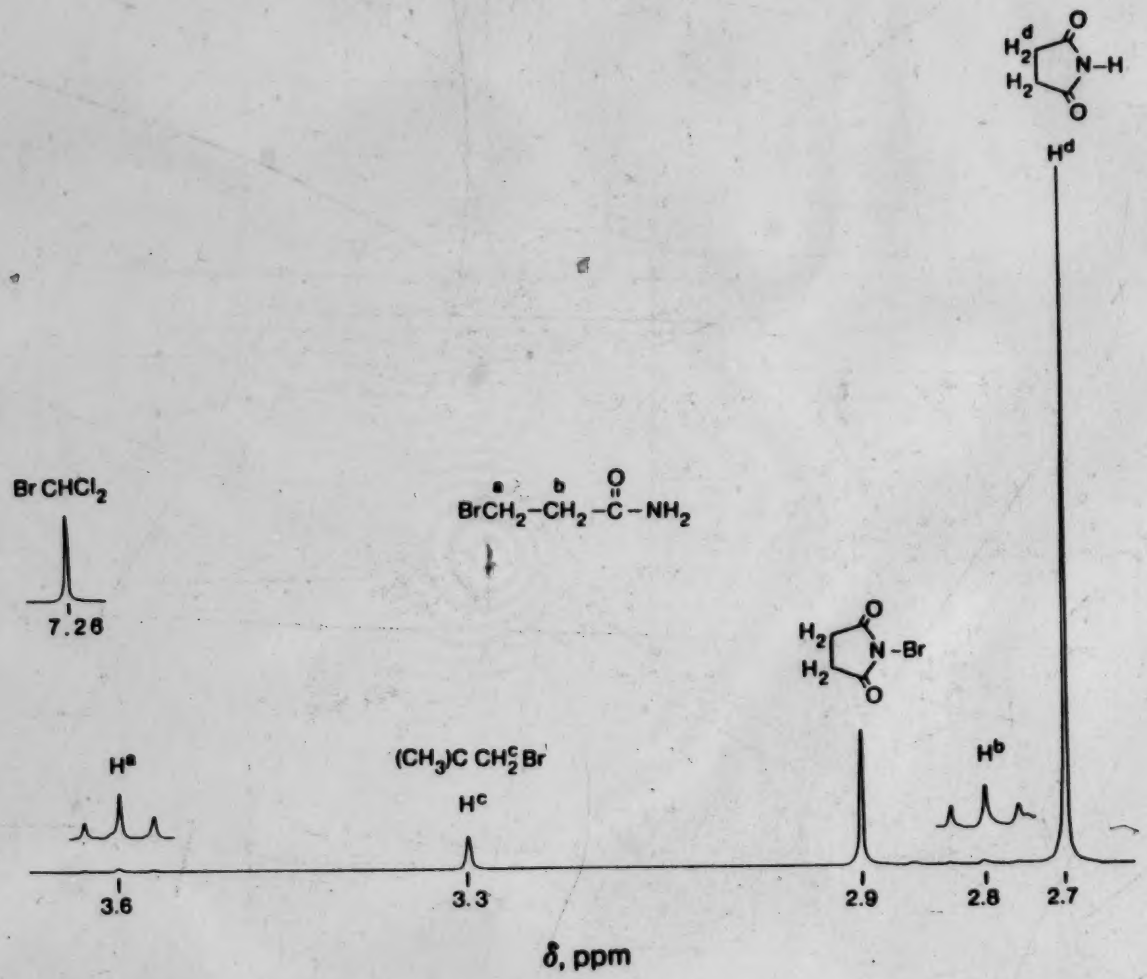


Figure 7. 200 MHz ^1H NMR Spectrum of the Reaction Product Mixture from the Photobromination of Neopentane and Dichloromethane with NBS-Br_2 (5/1).

detection are obvious. In all of the analyses in this report, since addition of small quantities of water was shown to quantitatively convert the β-BPIC to β-BPA (see Figures 8 and 9), water was added and the β-BPA formed was measured.

An alternative explanation for the failure to observe β-BPIC in the reactions where large amounts of bromine were added to the NBS bromination mixture, was that under those conditions a complexed radical such as proposed[125] (34 or 35) is the reactive species and cannot form β-BPIC. At the concentrations of bromine studied in this work (comparable to Skell's[119]) however, no evidence was observed for complex formation in this system.

If two competing radicals, succinimidyl and bromine atoms, are present with the NBS-Br_2 reagent, then using the r value obtained it should be possible to calculate the portion of the propagation sequence involving the succinimidyl radical and hence predict the amount of β-BPIC which should be present. Using equation 52 (see Appendix III for derivations of equations 52 and 53)

$$X_{NS\cdot} = \frac{(r_{obs.} - r_{Br\cdot})(r_{NS\cdot} + Q^{-1})}{(r_{NS\cdot} - r_{Br\cdot})(r_{obs.} + Q^{-1})} \qquad (52)$$

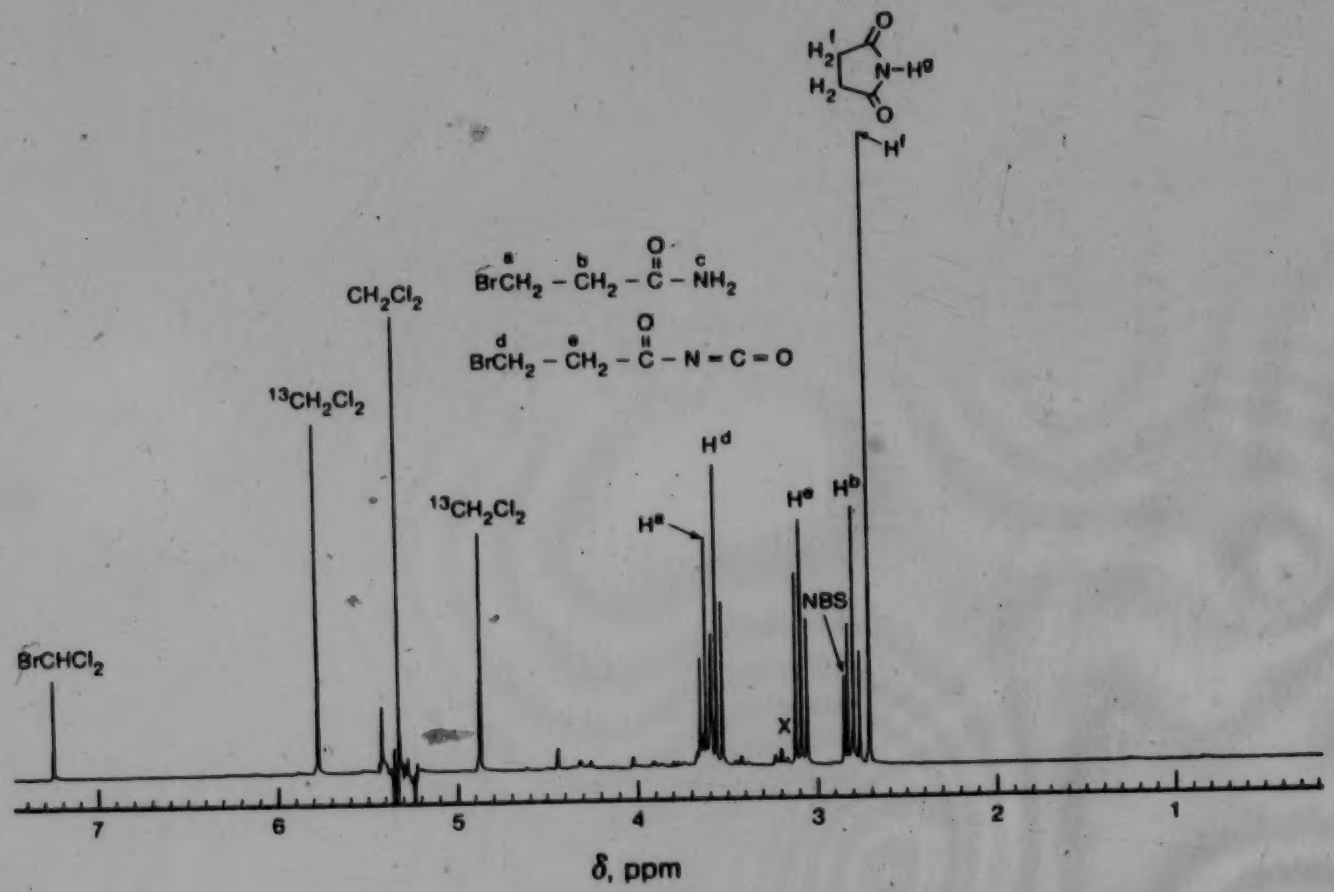


Figure 8. 200 MHz ^1H NMR Spectrum of the Reaction Product Mixture from the Photobromination of Dichloromethane with NBS-vinylidene Chloride (X = unknown).

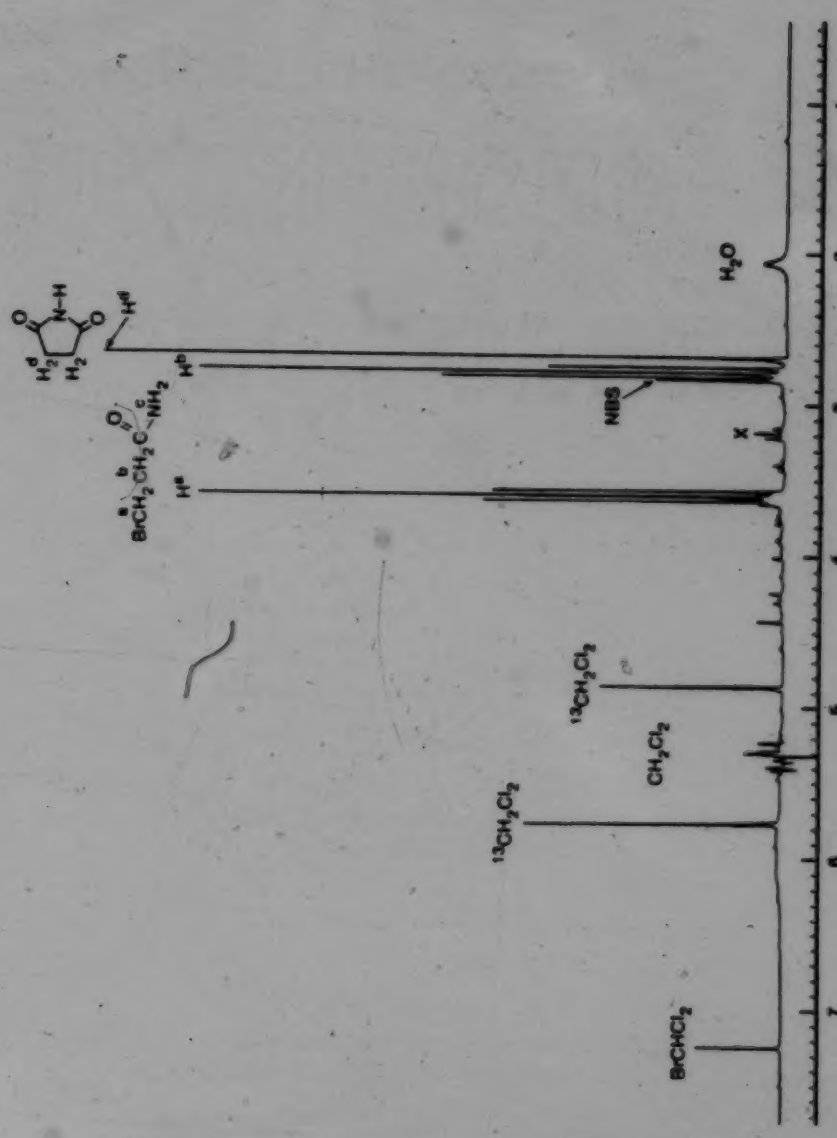


Figure 9. Results of Figure 8, after the Addition of 1 microliter of Water (X = unknown).

where r_{obs}, $r_{Br\cdot}$ and $r_{NS\cdot}$ are the observed, bromine atom ($r = 0.056$) and succinimidyl radical ($r = 19$) relative reactivities/H and Q is the ratio $[C_5H_{12}]x6/[CH_2Cl_2]$, it was possible to calculate $X_{NS\cdot}$, the average mole fraction of brominated substrate arising from abstraction by a succinimidyl radical. Using equation 53 where T is the

$$\left[BrCHCl_2\right]_{NS\cdot} = \frac{T \cdot X_{NS\cdot}}{(Q \cdot r_{NS\cdot}) + 1} \qquad (53)$$

total concentration of brominated substrates it was possible to calculate $[BrCHCl_2]_{NS\cdot}$, the bromodichloromethane arising from succinimidyl radical abstraction. If only one succinimidyl radical is in solution the ratio $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$ should be a constant under any reaction conditions. The results obtained for these calculations using data from Tables XVII, XVIII, and XIX are given in Table XXVI.

The average ratio, $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}] = 0.044 \pm 0.024$, obtained is higher than the value reported for σ-succinimidyl radical (~0.023),[123] but within the experimental error is the same. The range of r values for which the ratios, $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$, were calculated (0.1 to 18) covers the reported r values for the three

Table XXVI. $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$ Values Calculated Using Data from Tables III, IV and V.

Reagent		Substrates				
Additive	[NBS]/[Additive]	CH_2Cl_2/C_5H_{12}, mmol/mmol	r	$X_{NS\cdot}$	$[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$[a]	$r_{calc.}$[e]
None	0.104	31.2/3.92	1.44	0.537[b](0.525)[c]	0.026[b](0.028)[c]	2.41
	0.104	31.2/3.92	1.03	0.443	0.033	1.01
	0.104	31.2/3.92	0.965	0.425	0.023	1.85
	0.104	31.2/3.96	0.517	0.270	0.037	0.45
	0.104	31.2/3.92	0.432	0.229	0.026	0.561
	0.104	31.2/3.90	0.276	0.147	0.020	0.462
	0.104	31.2/3.92	0.138	0.0600	0.018	0.211
	0.104	31.2/3.90	0.127	0.0522	0.018	0.191
Ethylene	0.099/0.011	31.2/0.38	17.8	0.972	0.032	18.4
	0.099/0.011	31.2/0.38	18.3	0.984	0.038	13.0
	0.099/0.011	31.2/0.38	17.9	0.975	0.032	19.2
	0.101/0.0113	31.2/0.38	22.9	---[d]	---[d]	---[d]
	0.101/0.0113	31.2/0.38	12.8	0.830	0.029	16.1
	0.101/0.0113	31.2/0.38	12.7	0.827	0.032	13.5
	$0.102/8.57\times10^{-4}$	31.2/4.32	0.971	0.449	0.025	1.62
	$0.104/1.95\times10^{-4}$	31.2/3.90	5.25	0.847	0.059	1.13
	$0.104/1.96\times10^{-4}$	31.2/3.92	3.68	0.777	0.049	1.32
	$0.104/2.05\times10^{-4}$	31.2/3.88	0.888	0.401	0.032	0.894
	$0.104/2.22\times10^{-4}$	31.2/3.88	0.469	0.245	0.023	0.743
	$0.104/1.68\times10^{-4}$	31.2/3.90	0.434	0.230	0.053	0.266
Bromine	$0.113/9.03\times10^{-4}$	15.6/2.16	0.150	0.0741	0.049	0.187
	$0.113/9.03\times10^{-4}$	15.6/2.18	0.224	0.126	0.042	0.181
	$0.105/9.98\times10^{-4}$	31.2/4.37	0.397	0.229	0.017	0.970
	$0.105/9.98\times10^{-4}$	31.2/4.37	0.305	0.177	0.015	0.741
	$0.105/9.98\times10^{-4}$	31.2/4.32	0.202	0.111	0.018	0.347
	$0.105/9.98\times10^{-4}$	31.2/4.34	0.459	0.259	0.021	0.806

continued.....

Table XXVI (continued):

$0.102/1.13\times10^{-3}$	31.2/4.33	0.560	0.305	0.17	0.130
$0.102/1.13\times10^{-3}$	31.2/4.33	0.303	0.175	0.13	0.112
$0.102/1.32\times10^{-3}$	15.6/2.18	0.260	0.150	0.060	0.160
$0.104/1.50\times10^{-3}$	31.2/4.32	0.637	0.337	0.037	0.535
$0.104/1.50\times10^{-3}$	31.2/4.28	0.0894	0.0273	0.0080	0.203
$0.104/1.50\times10^{-3}$	31.2/4.36	0.0750	0.0150	0.0090	0.117
$0.103/2.29\times10^{-3}$	31.2/4.32	0.170	0.0885	0.059	0.116
$0.103/2.29\times10^{-3}$	31.2/4.32	0.151	0.0748	0.055	0.111
$0.103/2.29\times10^{-3}$	31.2/4.32	0.161	0.0821	0.058	0.113
$0.102/4.33\times10^{-3}$	31.2/4.33	0.124	0.0547	0.042	0.109
$0.102/4.33\times10^{-3}$	31.2/4.33	0.215	0.120	0.084	0.114
$0.106/2.12\times10^{-2}$	31.2/4.34	0.216	0.121	0.14	0.0896
$0.106/2.12\times10^{-2}$	31.2/4.34	0.288	0.166	0.25	0.0817
$0.103/2.06\times10^{-2}$	31.2/4.33	0.0560	--- [d]	--- [d]	--- [d]
$0.103/2.06\times10^{-2}$	31.2/4.33	0.0552	--- [d]	--- [d]	--- [d]

a. The overall average ratio $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$ = 0.049±0.030, the average for NBS = 0.025±0.005, the average for NBS-ethylene = 0.037±0.009, and the average for NBS-Br_2 = 0.066±0.047.

b. Results were calculated using $r_{NS\cdot}$ = 19 and $r_{Br\cdot}$ = 0.056.

c. Results in parentheses are calculated using $r_{NS\cdot}$ = 17 and $r_{Br\cdot}$ = 0.1 (taken from ref. 123).

d. Could not be calculated, since the values were outside the average parameter used and would give indeterminate solutions.

e. Calculated using eq. 54.

proposed abstracting species[119] (σ-NS$\cdot$, r = 21.3; π-NS$\cdot$, r = 1.15; Br$\cdot$, r = 0.1). Most of the scatter in the calculated ratios arises from the NBS-Br_2 reagent (see Table XXVI). The greater scatter with this reagent may be due to a larger uncertainty in the measurement of the small amounts of β-BPIC which were formed under these conditions. It also should be noted however, that during a kinetic investigation by Dauben,[136] the results obtained were found to be highly dependent upon small amounts of impurities present in the reaction mixtures. If an alternative possibility is considered, competing σ- and π-NS$\cdot$ chains, then the lowest obtainable value of r should approach 1.15, and values smaller than this should not have been possible. Since values smaller than 1.15 were obtainable with all three reagents (NBS, NBS-ethylene, and NBS-Br_2), this can be cleanly disregarded.

If a third radical species, which could abstract hydrogens from dichloromethane, but could not produce β-BPIC, were present it would increase the ratio $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$, since the calculation only corrects for bromine atoms. Since the value of $[BrCHCl_2]/[\beta\text{-BPIC}]$ for such a radical is infinite, if it were a significant competitor for the propagation sequence a large increase in the observed ratio $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$ would be expected. It is significant that data

which gave r values (1.44-0.888) near 1.15, the value for π-succinimidyl,[119] also gave ratios $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$ between 0.023 and 0.033.

Equation 52 can also be derived from the rate expressions for the reactions in Scheme XI, and pre-

$$NS\cdot + C_5H_{12} \xrightarrow{k_1} \longrightarrow C_5H_{11}Br$$

$$Br\cdot + C_5H_{12} \xrightarrow{k_2} \longrightarrow C_5H_{11}Br$$

$$NS\cdot + CH_2Cl_2 \xrightarrow{k_3} \longrightarrow CHCl_2Br$$

$$Br\cdot + CH_2Cl_2 \xrightarrow{k_4} \longrightarrow CHCl_2Br$$

$$NS\cdot \xrightarrow{k_5} \longrightarrow \beta\text{-BPIC}$$

Scheme XI

sented in the form of equation 54 (see Appendix III).

$$r = \frac{1}{8} \cdot \frac{(k_1/k_5)\left((k_2/k_4)\left[C_5H_{12}\right] + \left[CH_2Cl_2\right]\right) + (k_2/k_4)\left(\frac{1}{Y} - \frac{1}{Y_S}\right)}{(k_3/k_5)\left((k_2/k_4)\left[C_5H_{12}\right] + \left[CH_2Cl_2\right]\right) + \left(\frac{1}{Y} - \frac{1}{Y_S}\right)} \qquad (54)$$

The ratio of the yield of β-BPIC to the yield of total products for a pure succinimidyl radical chain is defined as Y_S, and Y is that same ratio which is experimentally observed. The advantage of this approach was to demonstrate that the kinetic observations are not dependent upon the time related ratio of the two radicals.

Using equation 54 and the data from Tables XVII, XVIII and XIX the value of $r_{calc.}$ can be compared with the experimentally observed values (see Table XXVI). The two sets of r values are correlated linearly, with a slope of 0.97±0.04 showing a correlation coefficient, r, of 0.97.

Since r can be described by an equation involving only two abstracting species, NS· or Br·, any mechanistic interpretation based on the relative magnitude of r values obtained experimentally, which utilizes more than one abstracting succinimidyl radical, is not demanded.

Qualitatively the results obtained appear to accurately describe the kinetics defined by Scheme XI, however an analysis of the experimental data using equation 54, i.e. a plot of $(1/Y-1/Y_s)/((k_3/k_5)(k_2/k_4[C_5H_{12}]+[CH_2Cl_2])+(1/Y-1/Y_s))$ vs r_{obs}, shows a poor correlation. An analysis of the magnitude of the range of experimental error in the values used ($r_{NS\cdot}$ = 19±1.7, $r_{Br\cdot}$ = 0.056 ± 0.007, $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$ = 0.032 ± 0.006) to evaluate the kinetic parameter, r, was shown to invalidate any meaningful conclusions based on these kinetics, since the uncertainty in the calculated values of r encompassed all but one of the experimentally observed points (see Appendix IV).

A key point in the argument for two reactive states

of the succinimidyl radical was the similarity of r values obtained with NBS-Br_2 and NIS-I_2, and the reported observation that ring opening to the isocyanate radical did not occur with these two reagents.[119] Table XX presents results which indicate 72-75% yields of β-IPIC, contradictory to previous reports[119-122] (see Figure 10). The relative reactivities obtained with the NBS-ethylene reagent suggested a value of r ~19 for abstraction from neopentane and dichloromethane by a succinimidyl radical. Since abstraction by iodine atoms would be energetically unfavorable,[137] the abstracting species responsible for the relative reactivities observed with the NIS-I_2 reagent, 0.716-0.784, is not clearly defined. As was mentioned in the results section the synthetic iodides ($C_5H_{11}I$ and $ICHCl_2$) were found to be unstable to light. This may mean that the r values obtained with this reagent are an artifact of the product instabilities. Assuming values of r = 19 and [$ICHCl_2$]/[β-IPIC] = 0.044 for succinimidyl radical, a calculation of the β-IPIC expected indicates that too much ring opened product was produced. This suggests that if succinimidyl radical is involved in this system, it is not the only species present.

A tentative explanation for the results obtained with the NIS-I_2 reagent is that a complex radical such as

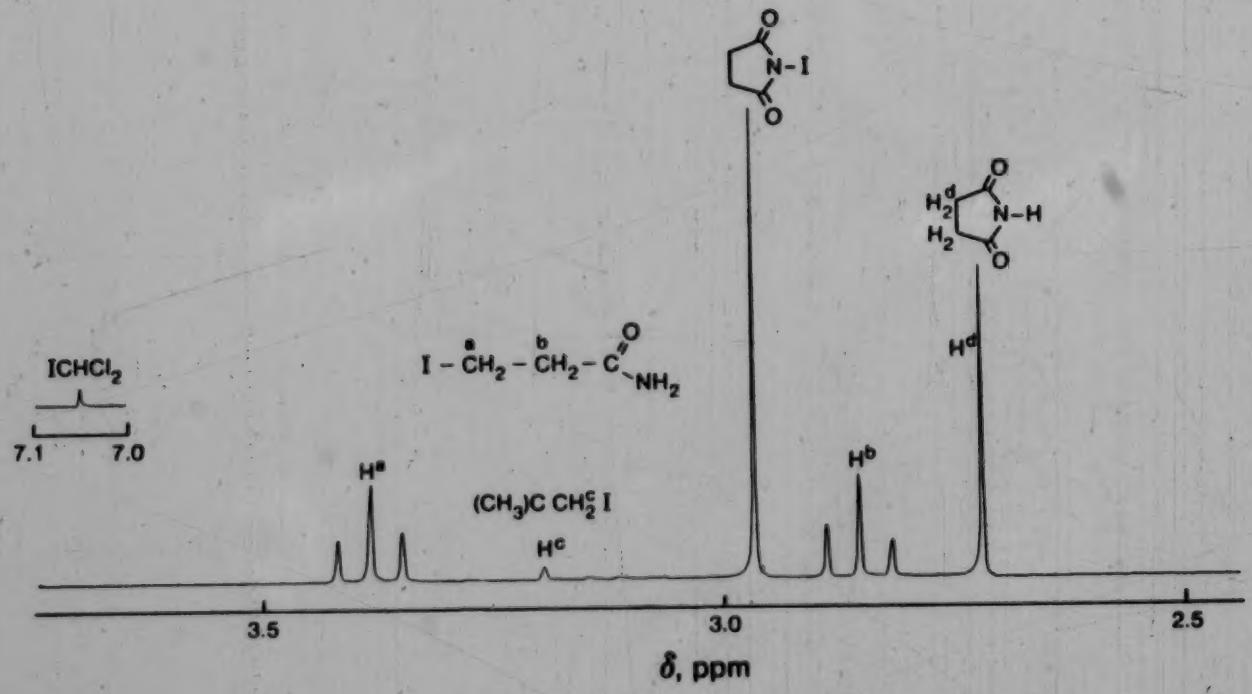
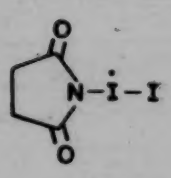
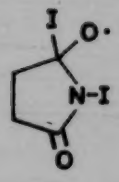


Figure 10. 200 MHz ^{1}H NMR Spectrum of the Reaction Product Mixture from the Photoiodination of Neopentane and Dichloromethane with NIS-I_2.

37 or 38 (similar to those suggested for NBS-Br_2[125]) is

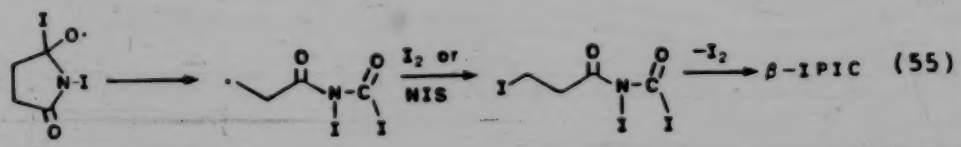


37



38

present in this system. Radical intermediates similar to 37 are well known in other systems; from iodobenzene dichloride,[138] tert-butylhypoiodite,[139] and from reduction of diaryliodonium salts.[140] Complexed radical 38 has the added advantage of an alternative direct route to β-IPIC, equation 55. This alternate pathway would easily explain the higher than predicted yield of β-IPIC.



(55)

The relative reactivities observed may therefore be due to one of these complexed radicals or a competition between a succinimidyl radical and one of these complexed radicals.

VII.3 The Graded Series

The proposal was made[123] that the ratio of $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained, in the reaction of the NBS-vinylidene chloride reagent with dichloromethane in the presence of a variety of added substrates, would be a constant if only one abstracting species were present. Alternatively if two competing chains, σ- and π-succinimidyl radical, were present the ratio was predicted to increase as more π-succinimidyl radical is involved, since this radical was proposed to be unable to rearrange to the β-propionyl isocyanate radical. Based on the results obtained, the original report[123] concluded that two abstracting species were involved, since the ratio of $[BrCHCl_2]/[\beta\text{-BPIC}]$ was found to change with the substrate added.

In this investigation the ratio $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained for all of the added substrates, except benzene, is essentially a constant, 0.046 ± 0.017 (see Table XXI). This value is also in good agreement with the average calculated value of $[BrCHCl_2]_{NS.}/[\beta\text{-BPIC}]$, 0.044 ± 0.024, found for the reactions of NBS with neopentane and dichloromethane. In the reactions with added cyclohexene or 1,3-butadiene large amounts of the products of addition of NBS to the double bonds (1-bromo-2-succinimidyl-

cyclohexane, or 3-bromo-4-succinimidyl-1-butene and 1-bromo-4-succinimidyl-2-butene) were formed as was reported.[123] Contrary to the initial report, however, only trace amounts of bromodichloromethane were observed to have formed, although similar signals were observed in the nmr spectra for these reactions (benzene in the cyclohexene, and unidentified impurities in the 1,3-butadiene). This discrepancy is therefore, most likely, due to misassignment of the nmr signals to bromodichloromethane. This finding supports the conclusion that the addition of the olefinic substrates serves to keep the concentration of bromine to a minimum, but at the same time traps large quantities of succinimidyl radicals. This greatly reduces the concentration of succinimidyl radical in solution, and as a result, lowers the yield of β-BPIC and $BrCHCl_2$ observed. The ratio $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained, although more uncertain because of the small quantities measured, is within the experimental error, the same as measured for the other substrates. In contrast to the original report,[123] regardless of the added substrate, only one succinimidyl radical is concluded to be present, presumably the ground state.

VII.4 Photobrominations in the Presence of Benzene

In contrast with the other substrates added to the reaction of NBS-vinylidene chloride in dichloromethane, the addition of benzene produced a large ratio of $[BrCHCl_2]/[\beta\text{-BPIC}]$ (0.164-2.18). The high values of $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained with added benzene appear to be the result of an added scavenger; this time however, an efficient trap for the succinimidyl radical. Originally, olefin was used to trap the bromine atom, however as can be seen from the previous results, Table XVIII, the olefin serves this function, but is not highly efficient, as in the case of allylic bromination. On the other hand, it appears that high concentrations of benzene competitively trap succinimidyl radicals, as can be seen from the high yields of products resulting from its addition to benzene (greater than the products resulting from addition of bromine to olefinic materials), see reaction 12, Table XXI. The competitive abstraction by the two radicals, $Br^{\bullet}$ and $NS^{\bullet}$, moderated by their relative concentrations, yield ratios which should be dependent upon the relative concentrations of the added trapping agents. This proposal is consistent with the higher values of $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained by increasing the benzene concentration (i.e. the $NS^{\bullet}$ trap),

while an increase in the amount of vinylidene chloride (i.e. the Br· trap) results in lower values of this ratio (see Table XXII). The previous suggestion that the two competing species were π- and σ-succinimidyl radical, is not consistent with the lower values of $[BrCHCl_2]/[\beta\text{-BPIC}]$ obtained with an increase in the vinylidene chloride, since this olefin has been suggested to be a poor trap for the π-succinimidyl radical.[123] The competitive abstraction by bromine atoms is further attenuated by the fact, that added benzene, following the recipe previously reported,[123] yielded insoluble NBS which favors the incursion of the bromine atom chain (see Table XIII).[110,127] A calculation of $X_{NS\cdot} = ([BrCHCl_2]_{NS\cdot} + [\beta\text{-BPIC}])/([BrCHCl_2]_{total} + [\beta\text{-BPIC}])$ allows the estimation of the fraction of the reaction which proceeded by the bromine atom chain. This calculation indicates that a ratio, $[BrCHCl_2]/[\beta\text{-BPIC}]$, of 0.164 (see Table XXII) would arise from a competition where 10% of the brominated products are the result of abstraction bromine atoms and a ratio of 2.18 (see Table XXII) would occur when 67% of the brominated products are the result of abstraction by bromine atoms.

VII.5 Brominations of Chloroform

It was suggested[123,124] that the NBS-olefin reagent behaved in a different manner in the solvent chloroform than it did when the reaction was carried out in dichloromethane. The proposal made, was that the trichloromethyl radical was stable enough that only the π-radical could be formed through transfer with NBS, and that consequently no β-BPIC would be observed in the products.

The yield of β-BPIC obtained during the photobromination of chloroform with the NBS-olefin reagent (see Table XXIII) does not agree with the results reported previously,[123,124] but agrees well with the results reported by Walling.[125] It had been suggested[124] that large yields of β-BPIC would be obtained if the reaction was not properly degassed (i.e. by flushing with argon), however with proper degassing (freeze-thaw vacuum technique) no β-BPIC would be observed. This suggestion does not appear to be correct, since the results presented here were obtained from samples which had been degassed by the freeze-thaw vacuum technique.

Qualitatively the behavior of NBS in chloroform is almost identical to that in the neopentane/dichloromethane mixtures. In neopentane/dichloromethane mixtures

the NBS-ethylene reagent reacts almost exclusively by a succinimidyl radical chain to give a low yield of brominated substrates and a high yield of β-BPIC, the NBS-bromine reagent reacts almost exclusively by a bromine atom chain to give high yields of brominated substrate and a low yield of β-BPIC, and NBS alone gives intermediate values. Qualitatively the same behavior must occur in chloroform since the NBS-olefin reagent gives high yields of β-BPIC (82.7%) and low yields of bromotrichloromethane (1.38%) (see Figure 11), the NBS-Br_2 reagent gives low yields of β-BPIC (2.31%) and high yields of bromotrichloromethane (101%) (see Figure 12), and NBS alone gives results in between (% yield β-BPIC = 19.8, $BrCCl_3$ = 85.5). Based on this similarity, it does not appear that using chloroform as the solvent has any appreciable effect upon the reaction mechanism using the three reagents (NBS-olefin, NBS, or NBS-bromine). It does, however appear from the results in Table XXIV that some of the β-BPIC obtained is photochemical in origin. Further evidence that solvent chloroform does not change the reaction mechanism is the observation that addition of chloroform to the neopentane/dichloromethane reactions, in quantities large enough to be a competing substrate, does not appreciably change the results obtained compared to those obtained in its absence (see Appendix II).

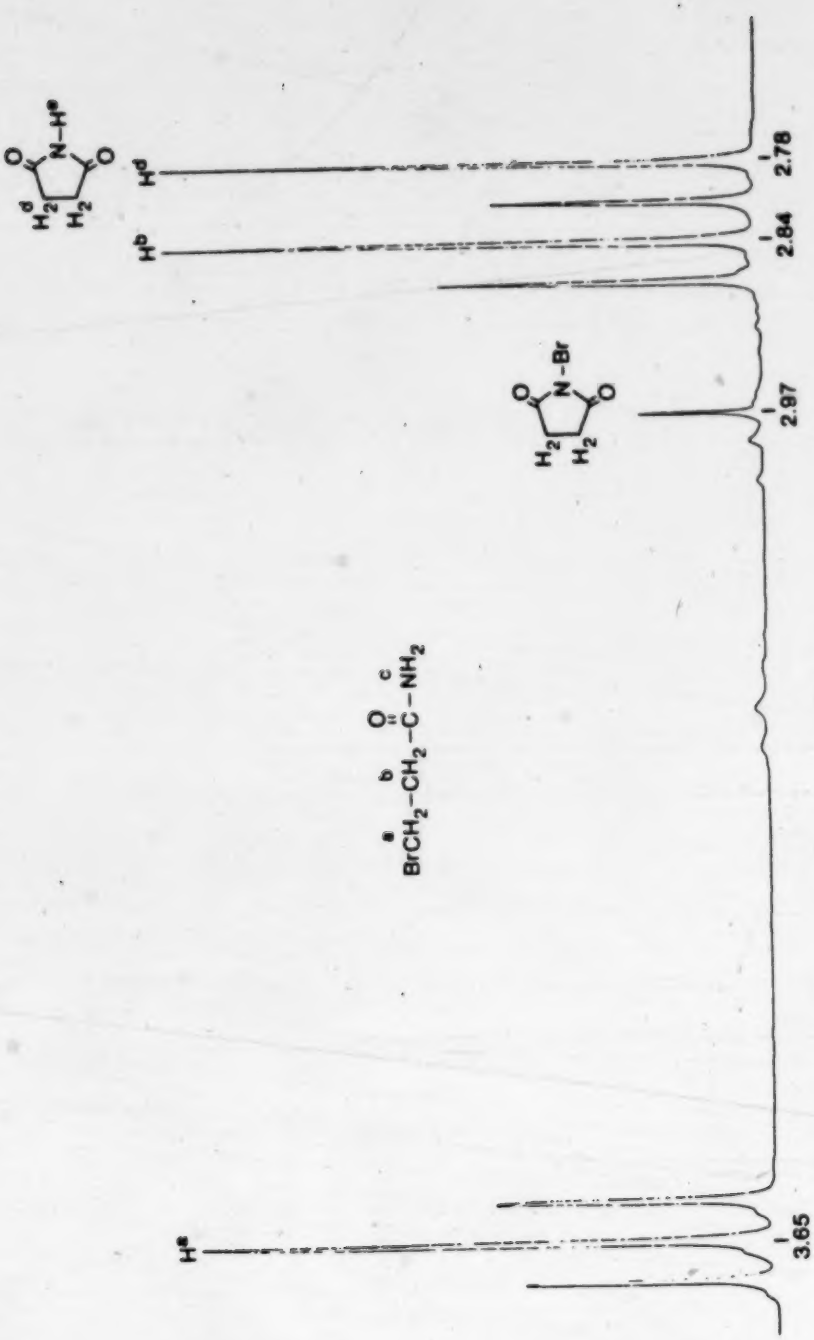


Figure 11. 200 MHz ^{1}H NMR Spectrum of the Reaction Product Mixture from the Photobromination of Chloroform with NBS-vinylidene Chloride.

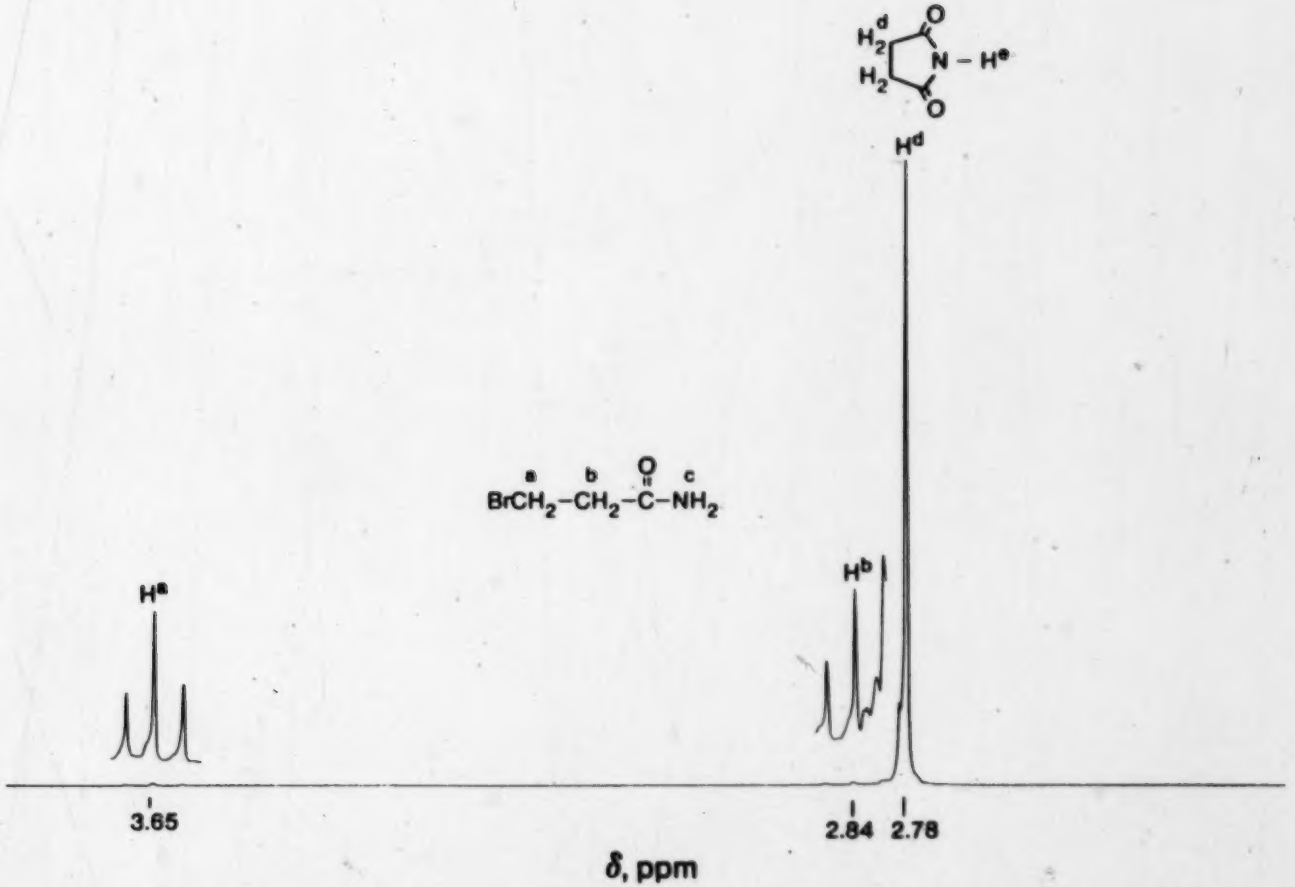


Figure 12. 200 MHz ^{1}H NMR Spectrum of the Reaction Product Mixture from the Photobromination of Chloroform with NBS-Br_2.

VII.6 Photoiodination of Chloroform with NIS-Iodine

Use of chloroform as the solvent and use of the NXS/X_2 reagent have been proposed to be methods of generating π-succinimidyl radical based on the total absence of β-XPIC in the product mixtures.[119-124] The observation that yields of 69 to 75% of β-IPIC are obtained from NIS-iodine in chloroform is in direct conflict with this proposal (see Figure 13). This system encompasses both of the suggested requirements, and yet large yields of β-IPIC are formed, which has been proposed to arise only from σ-succinimidyl radical. By comparison with the results obtained in the neopentane/dichloromethane reaction with this reagent, the results obtained are proposed to arise from a complex radical (37 or 38) as suggested previously for the other system.

VII.7 Mechanistic Conclusions

The results obtained from the photobrominations of cyclopentane and cyclohexane with the NBS containing reagents showed a variety of relative reactivities, and can be described by a mechanism involving competing succinimidyl radical and bromine atom chains. The dominance of each of the chain-carrying processes depends upon the solvent used, and upon the additives (molecular

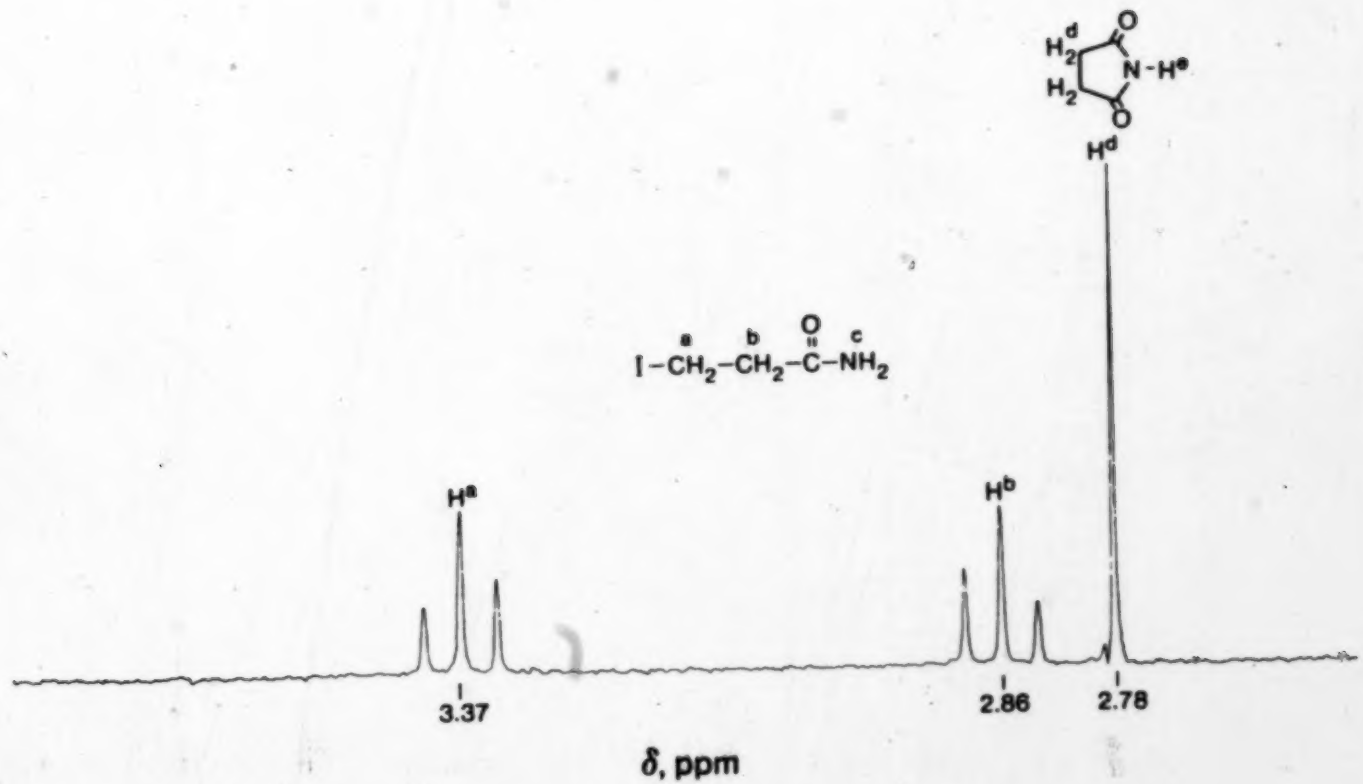


Figure 13. 200 MHz ^{1}H NMR Spectrum of the Reaction Product Mixture from the Photoiodination of Chloroform with NIS-I_2.

bromine or ethylene) used to moderate or enhance one or the other of the chain processes. The abstraction sequence is accompanied by a competing rearrangement reaction of succinimidyl radical to β-BPIC. β-BPIC was observed to be formed under all of the reaction conditions studied.

Two criteria were used to justify the original proposal,[119] that two thermally accessible states of succinimidyl radical were involved in the competitive abstraction reactions from neopentane and dichloromethane. These were an observed change in the obtained value of r with the reagent employed (NBS-olefin, NBS-Br_2 or Br_2), and the presence or absence of β-BPIC in the product mixtures obtained from the NBS containing reagents. The observations in this study were that the relative reactivity, r, changes with percentage conversion of NBS as well as with added materials (molecular bromine or olefin), that the values of r obtained encompass the reported values attributed to both states of the succinimidyl radical, and that β-BPIC is formed under all reaction conditions. These results allow the reaction mechanism to be described by competing succinimidyl radical and bromine atom chains as is proposed for the reactions with the substrates cyclopentane and cyclohexane. By using the observed value of r to predict the

fraction of the abstraction occurring from succinimidyl radical, the calculated ratio $[BrCHCl_2]_{NS\cdot}/[\beta\text{-BPIC}]$ could be obtained. This ratio, under all of the conditions studied, was found to be essentially a constant.

Contrary to the original report[123] the addition of a variety of substrates to the reaction of NBS-vinylidene chloride in dichloromethane did not show changing values of the ratio $[BrCHCl_2]/[\beta\text{-BPIC}]$. The addition of benzene did produce larger ratios of $[BrCHCl_2]/[\beta\text{-BPIC}]$ as was reported,[123] however this change appears to be the result of adding a scavenger for succinimidyl radicals which allows a competitive abstraction by bromine atoms and succinimidyl radicals to occur.

The reagent NIS-I_2 produces large yields of β-IPIC, contradictory to previous reports, in solvents dichloromethane or chloroform. The results obtained do not appear to support a reaction mechanism involving succinimidyl radical alone. The results obtained with this reagent are tentatively assigned to a complexed radical such as 37 or 38, or a competition between 37 or 38 and succinimidyl radical.

The succinimidyl radical, in no matter which state it is generated, would be expected to be rapidly thermolyzed by collision with solvent molecules to the ground state. Based on the theoretical work by Koenig[112]

and work presently in progress[116] which predict a small energy separation between the two states, the ground state is suggested to be in thermal equilibrium with an excited state in solution. The ring opening process to yield β-BPIC is therefore, assumed to occur from the excited state, in equilibrium with the ground state under all of the conditions studied.

EXPERIMENTAL

VIII.1 Materials

Perdeuteriocyclohexane (Merck, Sharp and Dohme, Canada) was used without further purification. Glpc analysis showed it to be >99.9% pure, and mass spectral analysis (AEI MS-50, 12 eV) showed it to contain 99.47 atom % D.

Cyclopentane (Phillips 66, research grade) and cyclohexane (Aldrich Chemical) were heated to reflux over P_2O_5 and fractionally distilled using an 18-in. Vigreux column. The middle fractions were collected. Glpc analysis showed them to be >99.9% pure.

Neopentane (Phillips 66, research grade, >99.9%) was distilled prior to use (for purification of neopentane shown by infrared analysis to contain olefin see reference 132).

Freon 112 (PCR) and Freon 113 (Matheson of Canada Ltd.) were fractionally distilled (18-in. Vigreux column) from P_2O_5; the middle fractions (Freon 112 bp 92°C, Freon 113 bp 47°C) were collected.

Bromine (Fisher Scientific) was washed twice with concentrated sulfuric acid, decanted, and fractionally

distilled (18-in. Vigreux column) from P_2O_5. The middle fraction was collected.

Iodine (Terochem Laboratories) was sublimed before use.

N-Bromosuccinimide (Fisher Scientific or MCB) was recrystallized from hot water. Titration with aqueous thiosulfate showed it to be more than 99.5% pure.

N-Iodosuccinimide (Arapahoe Chemicals) was recrystallized from hot acetone. Titration with aqueous thiosulfate showed it to be more than 99.2% pure.

Ethylene (Matheson, research grade >99.98%) was distilled (trap to trap) before use.

1,1-Dichloroethylene (Aldrich Chemical) was distilled (bp 30-32°C) under nitrogen immediately prior to use.

Acetonitrile (MCB) was purified by successive distillations from potassium permanganate and sodium carbonate. The distillate was treated with several drops of concentrated sulfuric acid and redistilled. Finally, it was distilled again from calcium hydride and stored in a flask which was sealed with a serum cap.

Benzene (American Chemicals Ltd.) was dried over sodium wire and distilled prior to use. Glpc analysis

showed it to be >99.9%.

Dichloromethane (Caledon Chemical Co.) was dried over calcium chloride and distilled using a 3-ft. Teflon spinning-band column. Glpc analysis showed it to be >99.98%. Traces of chloroform were detected.

Chloroform (American Chemicals Ltd.) was distilled through a 3-ft. Teflon spinning-band column. It was further distilled from P_2O_5 through an 18-in. Vigreux column immediately prior to use. Glpc analysis showed it to be >99.98%.

Cyclohexene (BDH) was dried over sodium sulfate, filtered and distilled through a 3-ft. stainless steel spinning-band column. Glpc analysis showed it to be 99.8%. Impurities were identified as benzene (0.13%) and 1,3-cylcohexadiene (0.07%).

1,3-Butadiene (Matheson, research grade >99.9%) was distilled prior to use (see results section).

2,3-Dimethylbutane (Phillips 66, research grade >99.88%) was used without further purification.

Di-tert-butylperoxyoxalate was prepared from tert-butylhydroperoxide and oxalyl chloride using the procedure of Bartlett.[141] The white needles obtained were stored in the dark at -20° until used.

α,α'-Azobisisobutyronitrile (Aldrich Chemical) was recrystallized from ethanol-water: mp 101-102°C [lit.[142] mp 103°C].

VIII.2 Instrumentation

Nmr spectra, 200 MHz ^1H, were obtained using a Bruker WH-200 nmr spectrometer, 80 MHz ^1H nmr spectra were obtained using a Bruker WH-80 nmr spectrometer and 60 MHz ^1H nmr spectra were obtained using a Varian A-56/60A nmr spectrometer. Glpc analyses were done using a Hewlett Packard 5840A gas chromatograph equipped with a flame ionization detector, calibrated using a mixture of the authentic materials plus the standard used, and a capillary injector system. Mass spectra were run using an AEI model MS-12 mass spectrometer.

VIII.3 Compounds

Neopentyl bromide was prepared from the photobromination of neopentane with a mixture of bromine and chlorine at 0°C in Freon 113. The solution was washed with aqueous thiosulfate, saturated aqueous sodium bicarbonate and dried over sodium sulfate. The Freon was removed by distillation and the residue was fractionated through a 6-in. Vigreux column to give a colorless

liquid: bp 103-104°C (710 mm) [lit.[143] bp 106°C (760 mm)]; 60 MHz ^1H nmr ($CDCl_3$) δ 1.05 (s, 9H), 3.40 (s, 2H).

Neopentyliodide was prepared from neopentane and tert-butylhypoiodite by the procedure of Tanner and Gidley.[144] The colorless liquid product was kept in the dark, since it rapidly turned a color characteristic of iodine upon exposure to room light: bp 39-41°C (30 mm) [lit.[145] bp 47-50°C (40-45 mm)];, 80 MHz ^1H nmr ($CDCl_3$) δ 1.07 (s, 9H), 3.19 (s, 2H).

Iododichloromethane was prepared from chloroform and methyliodide with aluminum trichloride following the procedure of Seyferth and Haas.[146] The colorless liquid product was kept in the dark since it rapidly turned a color characteristic of iodine upon exposure to room light: bp 120-126°C (710 mm) [lit.[147] bp 132°C (760 mm)]; 80 MHz ^1H nmr (CD_3CN) δ 7.10 (s).

Iodotrichloromethane was prepared from trichloroacetylchloride and hydrogen iodide following the procedure of Simons, Sloat and Meunier.[148] The colorless liquid product was stored in the dark since it rapidly turned a color characteristic of iodine upon exposure to room light: bp 124-126°C (690 mm) [lit.[149] bp 140-142°C

(760 mm)]; 80 MHz ^{1}H nmr (CD_3CN) no peaks; ir (neat) 745 cm^{-1} (s), 680 cm^{-1} (m).

β-Bromopropionamide was prepared from β-bromopropionic acid by heating to reflux with PCl_3 to yield the acid chloride, followed by reaction with ammonium hydroxide.[150] The precipitated product was washed 3 times with ice-cold water and dried: mp 110-113°C [lit.[151] mp 111°C]; 80 MHz ^{1}H nmr ($CDCl_3$) δ 2.75 (t, J = 7 Hz, 2H), 3.61 (t, J = 7 Hz, 2H), 6.20 (broad s, 2H).

β-Iodopropionamide was prepared from β-iodopropionic acid by refluxing with PCl_3 to yield the acid chloride, followed by reaction with ammonium hydroxide.[150] The precipitated product was dried by suction and recrystallized from acetonitrile: mp 135-136°C dec. [lit.[152] mp 140.5°C]; 80 MHz ^{1}H nmr ($CDCl_3$) δ 2.86 (t, J = 6.9 Hz, 2H), 3.37 (t, J = 6.9 Hz, 2H), 5.66 (broad s, 2H), mass spectrum m/e (rel intensity) 199 (29.1), 127 (12.9), 72 (98.2), 55 (7.8), 44 (100), 28 (16.4).
Anal. Calcd for C_3H_6INO: C, 18.11; H, 3.04. Found: C, 18.15; H, 3.03.

3-Bromocyclohexene was prepared by heating cyclohexane and NBS to reflux in carbon tetrachloride. The organic layer was washed with aqueous sodium thiosulfate

solution and water, and then dried over sodium sulfate. The colorless liquid product was obtained by fractional distillation: bp 84-86°C (42 mm) [lit.[153] bp 80-82°C (40 mm)]; 80 MHz ^1H nmr ($CDCl_3$) δ 2.11 (m, 6H), 4.85 (s, 1H), 5.85 (m, 2H); mass spectrum m/e (rel intensity) 81 (100), 80 (69.2).

4-Bromocyclohexene was prepared from 1,4-cyclohexanediol and PBr_3 heated to reflux in benzene according to the procedure of Fish and Broline:[154] bp 62°C (21 mm) [lit.[154] bp 50-52°C (22 mm)]; 80 MHz ^1H nmr ($CDCl_3$) δ 2.19 (m, 4H), 2.65 (m, 2H), 4.38 (m, 1H), 5.63 (m, 2H) [lit.[154] 90 MHz; δ 2.12 (m, 4H), 2.56 (m, 2H), 4.30 (m, 1H), 5.58 (m, 2H)]; mass spectrum m/e (rel intensity) 162 (9.5), 160 (10.1), 81 (94.8), 80 (100).

N-Phenylsuccinimide was prepared from succinic anhydride and aniline following the procedure of Cava, Deana, Muth and Mitchell.[155] The white needles obtained were recrystallized from 98% ethanol: mp 153-154°C [lit.[126] mp 150-152°C]; 200 MHz ^1H nmr (CD_3CN) δ 2.91 (s, 4H), 7.45 (m, 5H).

1-Bromo-2-succinimidylcyclohexane was isolated from a reaction of cyclohexene with NBS by extraction of the nonvolatile products with CCl_4 as a colorless liquid:

200 MHz ^1H nmr ($CDCl_3$) δ 1.19-2.23 (m, 8H), 2.72 (s, 4H), 4.13 (m, 1H), 4.83 (m, 1H) [lit.[126] 60 MHz δ 1.15-2.1 (m, 8H), 2.7 (s, 4H), 3.8-5.0 (m, 2H)]; mass spectrum m/e (rel intensity) 261 (1.6), 259 (1.7), 180 (2.0), 100 (100).

6-Succinimidyl-3,4,5-tribromocyclohexene was isolated from a reaction of benzene with NBS as described by Chow.[126] The white solid was separated by column chromatography on alumina using CCl_4/CH_2Cl_2: mp 194-204°C, dec. [lit.[126] mp 204-207°C]; Fourier transform ir 1700, 1190, 1160, 740 cm^{-1} [lit.[126] PE 457 grating spectrometer ir 1700, 1185, 1165, 780 cm^{-1}]; 200 MHz ^1H nmr ($CDCl_3$) δ 2.88 (s, 4H), 4.65-5.24 (m, 3H), 5.24-5.80 (m, 3H) [lit.[126] 60 MHz nmr 2.86 (s, 4H), 4.8-5.17 (m, 3H), 5.34-5.62 (m, 1H), 6.00 (m, 2H)]; mass spectrum m/e (rel intensity) 419 (0.2), 417 (0.7), 415 (0.8), 413 (0.4), 336 (7.6), 334 (15.1), 332 (8.1), 100 (100) [lit.[126] mass spectrum m/e (rel intensity) 419 (0.2), 417 (0.5), 415 (0.5), 413 (0.2)]. Exact mass calcd for $C_{10}H_8NBr_2O_2$: 335.88814, 333.89014, 331.89214. Found: 335.8879, 333.8895, 331.8911.

1-Bromo-4-succinimidyl-2-butene and 3-Bromo-4-succinimidyl-1-butene were identified by their reported ^1H nmr spectra[126] (NS-CH_2CH=$CHCH_2Br$ δ 2.68 singlet, NS-$CH_2CHBrCH$=CH_2 δ 2.85 singlet).

VIII.4 Analytical Procedures

Bromination of Cyclopentane and Cyclohexane with NBS. Aliquot samples of solutions, or mixtures of weighed quantities of NBS and the two substrates, or of the two substrates and an internal standard (hexachloroethane) dissolved in the suitable solvent, were placed in Pyrex ampoules. The reaction vessels were degassed by the freeze-thaw method, in the absence of light, and thermostated at 23 ± 0.5°C. After equilibration, the tubes were irradiated with incandescent light through the (9 mm) Pyrex thermostat for an appropriate period of time (approximately 16 h for 50% reactions). The reaction vessels were then quenched in liquid nitrogen and subjected to iodometric titration. An aliquot of a standard solution containing two external standards, o-dichlorobenzene and chlorobenzene, was added, and the organic mixture was analyzed by Glpc with either a 50 m methyl silicone capillary column, a 10-ft x 1/8-in. stainless steel column packed with 5% Ucon Polar HB50 2000 on Chromosorb PAW, or a 24-ft x 1/4-in. 7% SE-30 on Chromosorb PAW stainless steel column. The area ratios obtained from the chromatograms were determined by using a Hewlett-Packard integrator. The molar ratios of products to standards were determined from standard calibration curves. When the reactions were carried out

in acetonitrile, the standard was added as a solution in n-pentane so that the organic and aqueous phases were immiscible. Control experiments on synthetic product mixtures added to the reaction mixtures but isolated and analyzed without irradiation showed that the analytical procedure was accurate. Preanalyzed synthetic reaction mixtures, without brominating reagent, were irradiated, subjected to the analytical procedure, and found to give the same ratios of products (within the experimental errors quoted) as were found in the preanalyzed samples.

The reactions carried out with added bromine (irradiation times of 0.1 to 2 h for complete reaction) were carried out in an identical manner except that aliquots of standard solutions of molecular bromine in the required solvent were added to the reaction mixtures. The reactions with added bromine were carried out to various degrees of completion. The reactions were stopped when the active halogen remaining was still $> [Br_2]^o$.

The dibrominated cycloalkane, 1,2-dibromopentane, amounted to 7.1 ± 0.9% of the bromocyclopentane (CH_2Cl_2 solvent) and 3.3 ± 0.7% of the bromocyclopentane when the reactions were carried out in acetonitrile. Only traces of dibrominated cyclohexane were detected. When the reactions were carried out in CH_2Cl_2 as the solvent, 2.3 ± 0.5% of the active bromine produced $CHCl_2Br$.

The reactions run with added ethylene (irradiation times of ~20 h for 50% reaction) had manometrically measured amounts of ethylene transferred to the reaction vessel while the ampoule was still attached to the vacuum line.

Bromination of Cyclohexane and Perdeuteriocyclohexane with NBS and NBS-Br_2. The reactions were carried out and analyzed in the same manner as were the reactions of cyclohexane vs. cyclopentane. The molar concentration of NBS/C_6H_{12}/C_6D_{12} (0.079:0.071:0.071) or NBS/Br_2/C_6H_{12}/C_6D_{12} (0.079:0.014:0.071:0.071) (~50% reaction) ensured the best chance of observing any exchange reactions.

The unhalogenated hydrocarbons were isolated by preparative Glpc (SE-30 column), and the mixture of cyclohexane and perdeuteriocyclohexane was subjected to mass spectral analysis (AEI MS-2). A sample of the initial mixture of cyclohexane and perdeuteriocyclohexane and a sample of the mixture isolated after the reaction had identical mass spectral distributions of deuterated and protiated materials.

Vapor Phase Bromination of Neopentane and Dichloromethane. Mixtures of neopentane and dichloromethane were manometrically measured and transferred in vacuo to a break seal. Molecular bromine was weighed into a separate vessel equipped with a break seal, attached to a

vacuum line and degassed. The two break seals were attached to the reaction vessel (12 ℓ or 0.5 ℓ bulbs) and the break seals were opened in the absence of light in the order neopentane/dichloromethane, bromine, with 15 min. intervals between. The gaseous mixture was allowed to equilibrate for 1 h at 23° or 15°, and the vessel was irradiated with incandescent light (300 watts). The contents of the bulbs were condensed with liquid nitrogen into a tube attached to the reaction vessel and the sample was removed from the vacuum line. A dichloromethane solution of a standard, hexachloroethane, was added and the excess bromine and hydrogen bromide were destroyed with cold (0°) sodium bisulfite. The organic layer was analyzed by Glpc (50 m methyl silicone capillary column). A mixture of the reactants, with added amounts of a synthetic mixture of the products of bromination, was subjected to the reaction conditions, isolation and analytical conditions, with the exception that the mixture was never exposed to irradiation. The ratio of products, bromodichloromethane/neopentyl bromide, was the same (± 2.3%) as the original ratio of added products.

Solution Phase Bromination of Neopentane and Dichloromethane with Molecular Bromine. Solutions of molecular bromine in dichloromethane were placed in Pyrex

ampoules and attached to the vacuum line. Neopentane was measured manometrically and transferred to the reaction tubes. The ampoules were degassed and sealed and placed in the thermostat, in the absence of light. The reaction mixtures were allowed to equilibrate and were then irradiated through the Pyrex thermostat with a 400 watt General Electric sun lamp for the requisite time (~27 hr for complete reaction). The reaction tubes were frozen and the frozen mixtures were treated with a concentrated aqueous solution of sodium bisulfite to destroy the excess bromine. An aliquot sample of a dichloromethane solution of a standard, hexachloroethane, was added and the mixture was quantitatively analyzed by Glpc (50 m methyl silicone capillary column).

Mixtures of reactants also containing synthetic mixtures of products were placed under the reaction conditions, and isolation, and analytical procedures, but in the absence of light. A comparison of the relative ratios of products, from an analysis of the product mixtures before and after this procedure, showed them to be the same (± 2%). An aliquot sample, of a reaction mixture from a reaction carried out using 8 M bromine, was taken before the treatment with the bisulfite solution. The sample was frozen in liquid nitrogen and the mixture was treated with small amounts of 1-octene. The mixture was allowed to partially thaw, was refrozen

and the procedure was repeated until the bromine color had been discharged. An analysis of the product ratio from this procedure was the same (± 3%) as was found from the analysis of the remainder of the mixture using the aqueous bisulfite method of isolation. A preanalyzed dichloromethane solution of the bromination products, bromodichloromethane and neopentyl bromide, were thermostated (15°) and irradiated using the same apparatus as was used for the other liquid phase brominations of neopentane and dichloromethane. After a period of irradiation approximately twice as long as the other brominations, the reisolated products were reanalyzed and found to be the same (± 4%) as the preanalyzed product mixture.

The Photobromination of Neopentane and Dichloromethane with NBS in Solvent Dichloromethane. Mixtures of NBS, dichloromethane, and manometrically measured amounts of neopentane, were placed in Pyrex reaction ampoules, in the absence of light. The ampoules were degassed, sealed and thermostated at 15°. After equilibration the reaction vessels were irradiated in the same apparatus that was used for the reactions of these substrates with molecular bromine. When additives, ethylene or molecular bromine, were included they were added either as manometrically measured amounts (ethylene) or as aliquots of standard methylene chloride solutions (molecular

bromine).

After irradiation (~3 hr for complete reaction), the reaction tubes were frozen, opened, and the percentage reaction was determined by iodometric titration with sodium thiosulfate. An aliquot of a dichloromethane solution of a standard, hexachloroethane, was added and the mixture was quantitatively analyzed by Glpc (50 m methyl silicone capillary column).

Control experiments were carried out, in the same manner as for the brominations of these substrates with molecular bromine, and it was found that the isolation and analysis procedures gave an accurate (± 2%) determination of the relative reactivities reported.

The aqueous phase obtained subsequent to iodometric titration contained mixtures of β-bromopropionamide and succinimide.

Analyses of β-Bromopropionamide and Succinimide. For reactions where NBS had reacted to 100% completion a standard, butyramide, valeramide, or hexanamide, was added to the product mixture and the solution was analyzed using a 50 meter methyl silicone capillary column (150°-170°).

For reactions where NBS had reacted to <100% completion, the percentage reaction was determined by iodometric titration with aqueous thiosulphate. The

aqueous solution was separated from the organic layer. The water was distilled under reduced pressure, a standard was added to the residue, and the material which was soluble in acetonitrile was analyzed on the 50 meter methyl silicone capillary column (150°-170°C). Control experiments on standard mixtures of products substantiated the validity of the analytical procedure.

As indicated in Table XIX the [β-BPA] was also determined from the integrated areas of the methylene protons of β-BPA vs NSH (see Appendix V). The [NSH] having previously been determined by Glpc. Fourier transform 200 MHz ^1H nmr (40 scans, CD_2Cl_2 as solvent), gave product yields of β-BPA (±2%) which were within experimental error of those determined by Glpc (±4%).

Bromination of Perdeuteriodichloromethane and Neopentane in CCl_4 with Br_2 and HBr. A CCl_4 solution containing CD_2Cl_2 (1 M) and molecular bromine (0.24 M) was placed in a Pyrex ampoule. Neopentane and HBr were added manometrically, [neopentane] = 0.17 M, [HBr] = 0.25 M. The mixture was degassed, sealed, equilibrated at 15°C and irradiated.

The mixture was titrated iodometrically and found to have undergone 24.5% reaction. The remaining dichloromethane was collected by Glpc (6-ft. x 1/8-in. stainless steel column, n-octane/Porasil C, 100-120 mesh,

10 cc/min., 70°C), and samples of the original (before reaction) and recovered materials were submitted to mass spectral analysis. Based on the original and final ratios of m/e 89 to m/e 90, 1 mole % of protium was found to have been incorporated into the unreacted dichloromethane (approximately equal to one hydrogen reversal reaction for every four brominated dichloromethane product formed).

Bromination of Perdeuteriodichloromethane and Neopentane with NBS. A solution of NBS in perdeuteriodichloromethane was placed in a Pyrex ampoule. Neopentane was added manometrically in the absence of light and the ampoule was degassed, sealed, equilibrated at 15°C and irradiated.

Iodometric titration of the sample indicated the NBS had undergone 97.6% reaction. Mass spectral analysis of the original (before reaction) and the recovered materials indicated no incorporation of deuterium into the neopentane or of protium into the perdeuteriodichloromethane.

The Photoiodination of Dichloromethane and Neopentane with NIS and Iodine in Solvent Dichloromethane. Mixtures of NIS, I_2, dichloromethane, an internal standard, hexachloroethane, and manometrically measured amounts of neopentane were placed in Pyrex reaction

ampoules, in the absence of light. The ampoules were degassed, sealed and equilibrated at 15°C. After equilibration the reaction vessels were irradiated in the same apparatus used for the NBS reactions.

After irradiation (6 hrs for 80% reaction) the reaction tubes were frozen, opened, and a calculated amount of water was added (just sufficient to react with the β-IPIC). An aliquot sample was sealed in an nmr tube. A Fourier transform 200 MHz ^{1}H nmr spectrum of the sample was used for measurement of the yields of β-iodopropionamide and succinimide. The remaining solution was titrated iodometrically with aqueous sodium thiosulfate solution. The organic phase was separated, dried and analyzed for neopentyl iodide and iododichloromethane by Glpc (50 m methyl silicone capillary column).

The Reactions of the Graded Series with NBS in Solvent Dichloromethane. NBS and an internal standard, hexachloroethane, were weighed into Pyrex reaction ampoules and aliquot samples of mixtures of dichloromethane, 1,1-dichloroethylene, and the substrate of interest were added in the absence of light. The ampoules were degassed, sealed and thermostated at 15°C. After equilibration the reaction vessels were irradiated (20-30 hrs) in the same manner as the reactions of neopentane and dichloromethane.

After irradiation, the reaction tubes were frozen, opened, and a calculated amount of water was added (just sufficient to react with the β-BPIC). An aliquot sample was sealed in an nmr tube and analyzed by Fourier transform 200 MHz ^{1}H nmr for β-bromopropionamide and succinimide. The remaining solution was titrated iodometrically with aqueous sodium thiosulfate. The organic phase was separated, dried and analyzed by Glpc (50 m methyl silicone capillary column).

A standard mixture was prepared using the amounts of 1,2-dibromo-1,1-dichloroethane, 1,1-dichloroethylene, and dichloromethane present at 100% reaction (in a typical experiment carried out with added benzene) and an aliquot of this mixture was irradiated in the same apparatus for an equivalent length of time as in the experiments carried out with added benzene. Comparison of the pre-analyzed mixture and the reanalyzed mixture showed the 1,2-dibromo-1,1-dichloroethane to be stable to the reaction conditions (±4%), and no bromodichloromethane was found to have formed.

The Photobromination of Chloroform with NBS.

Mixtures of NBS and chloroform were placed in Pyrex reaction ampoules in the absence of light. When additives, 1,1-dichloroethylene or molecular bromine, were included they were added as aliquots of standard chloro-

form solutions. The ampoules were degassed, sealed, equilibrated at 15°C, and irradiated as described for the reactions carried out in solvent dichloromethane.

After irradiation (~3 hrs, 100% reaction) the reaction tubes were frozen, opened, a standard, carbon tetrabromide, was added, and the solution was analyzed in a similar manner to the reactions carried out in solvent dichloromethane. The yields of succinimide and β-bromopropionamide were determined by Fourier transform 200 MHz ^{1}H nmr. Bromotrichloromethane and hexachloroethane were determined by Glpc (50 m methyl silicone capillary column).

The Photobromination of Dichloromethane, Neopentane, and Chloroform with NBS. Mixtures of NBS, dichloromethane, chloroform and manometrically measured amounts of neopentane, were placed in Pyrex ampoules, in the absence of light. Bromine or ethylene were added as aliquots of solutions in dichloromethane and chloroform (bromine) or as manometrically measured amounts (ethylene). The ampoules were degassed, sealed and thermostated at 15°C. After equilibration the reaction vessels were irradiated in the same apparatus that was used for the neopentane/dichloromethane reactions.

After irradiation (~3 hrs, 100% reaction), the reaction tubes were frozen, opened, a standard, carbon

tetrabromide, was added, and the solution was titrated iodometrically with aqueous sodium thiosulfate. The bromodichloromethane, neopentylbromide, bromotrichloromethane and hexachloroethane were measured by Glpc (50 m methyl silicone capillary column). The β-bromopropionamide and succinimide were determined, as described for the neopentane/dichloromethane reactions, by Fourier transform 200 MHz ^1H nmr spectroscopy.

The Thermally Initiated Bromination of Chloroform with NBS. Mixtures of NBS, chloroform and either di-tert-butylperoxyoxalate (DBPO) or α,α'-azobisisobutyronitrile (AIBN) were placed in Pyrex reaction ampoules, in the absence of light. The ampoules were degassed, sealed and thermostated at the appropriate temperature (15°, 22.5°, 40°, or 60°).

After the reaction time had expired the reaction tubes were frozen and opened. The samples were analyzed for products in the same manner as the irradiated samples.

The Photoiodination of Chloroform with N-Iodosuccinimide and Iodine. Mixtures of NIS, I_2, and chloroform were placed in Pyrex reaction ampoules, in the absence of light. The ampoules were degassed, sealed and thermostated at 15°C. After equilibration the reaction vessels were irradiated as described for the NBS

reactions.

After irradiation (6 hrs, 80% reaction) the reaction tubes were frozen, opened, a standard, carbon tetrabromide, was added, and a calculated amount of water was added (just sufficient to react with the β-IPIC). An aliquot sample was sealed in an nmr tube and analyzed for succinimide and β-iodopropionamide by Fourier transform 200 MHz ^{1}H nmr spectroscopy. The remaining solution was titrated iodometrically with aqueous sodium thosulfate. The organic phase was separated, dried and analyzed for iodotrichloromethane and hexachloroethane by Glpc (50 m methyl silicone capillary column).

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distillation of a light petroleum fraction. The fraction with the highest purity was marketed as research grade >99.9% and contained traces of n-butane. A less pure fraction >99.6% was marketed as pure grade and contained n-butane and cis-butene-2 as identified impurities.

134. Neopentane was purified by irradiation in the presence of excess bromine, distillation and treatment with phenol, and vacuum distillation.

135. A slight bromine color was produced in these reactions. Some of the color persisted after titration with sodium thiosulfate.

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APPENDIX I. Product Identification and Measurement Method.

The product mixtures were analyzed by 400 MHz ^1H nmr spectrometry. For reactions run in hexachloroacetone, naphthalene was added as a standard before analysis. For reactions run in 15% CD_3CO_2D/85% H_2SO_4, o-dimethoxybenzene (veratrole) was added as a standard before analysis.

The yields of products were determined by measurement of the intensity of the absorption signals indicated below. The chemical shifts were assigned either from authentic product spectra or comparison to similar product spectra.

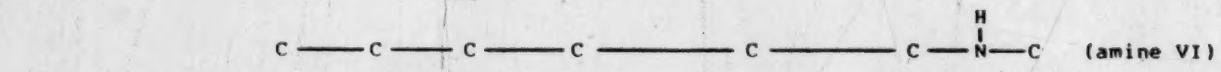
As an example of the method, 4-chloro-n-butyltrimethylammonium chloride showed a triplet for the protons on C-4, 3-chloro-n-butyltrimethylammonium chloride showed a doublet for the protons on C-4, and 2-chloro-n-butyltrimethylammonium chloride showed a triplet for the protons on C-4. Figure 2 gives a representative nmr spectrum for the product mixture from chlorination of ammonium salt III.

Location of Chlorine Atom

	C—C—C—C—$\overset{\oplus}{N}$—$(C)_3$						(Salt I)
Shift (ppm)	3.72	1.57	1.08	5.85-6.25[a]		5.65	
Type	t[b]	d	t	m		s	
Location measured	C4	C4	C4	C1		CN	
	C—C—C—C—C—$\overset{\oplus}{N}$—$(C)_3$						(Salt II)
Shift (ppm)	3.68	1.52	1.01	4.33-4.73[a]	5.75-6.15[a]	5.68	
Type	t	d	t	m	m	s	
Location measured	C5	C5	C5	C2	C1	CN	
	C—C—C—C—C—C—C—$\overset{\oplus}{N}$—$(C)_3$						(Salt III)
Shift (ppm)	3.59	1.48	1.05	4.05	4.35-4.75[a]	5.80-6.20[a]	5.74
Type	t	d	t	m	m	m	s
Location measured	C6	C6	C6	C3	C2	C1	CN
	C—C—C—C—C—N—$(C)_2$						(amine IV)
Shift (ppm)	3.45	1.39	0.86	4.06-4.46	5.46-5.86	5.29	
Type	t	d	t	m	m	d	
Location measured	C5	C5	C5	C2	C1	CN	
	C—C—C—C—C—$\overset{H}{\overset{\vert}{N}}$—C						(amine V)
Shift (ppm)	3.45	1.39	0.87	4.04-4.44	5.45-5.85	5.22	
Type	t	d	t	m	m	t	
Location measured	C5	C5	C5	C2	C1	CN	

continued.....

Location of Chlorine Atom (continued):



(amine VI)

Shift (ppm)	3.44	1.35	0.86	3.86	4.03-4.43	5.44-5.84	5.28
Type	t	d	t	m	m	m	t
Location measured	C6	C6	C6	C3	C2	C1	CN

a. No authentic material was available for comparison. The shift given was estimated based on the shift observed for chlorination at other locations.
b. t, d, s and m signify triplet, doublet, singlet and multiplet respectively.

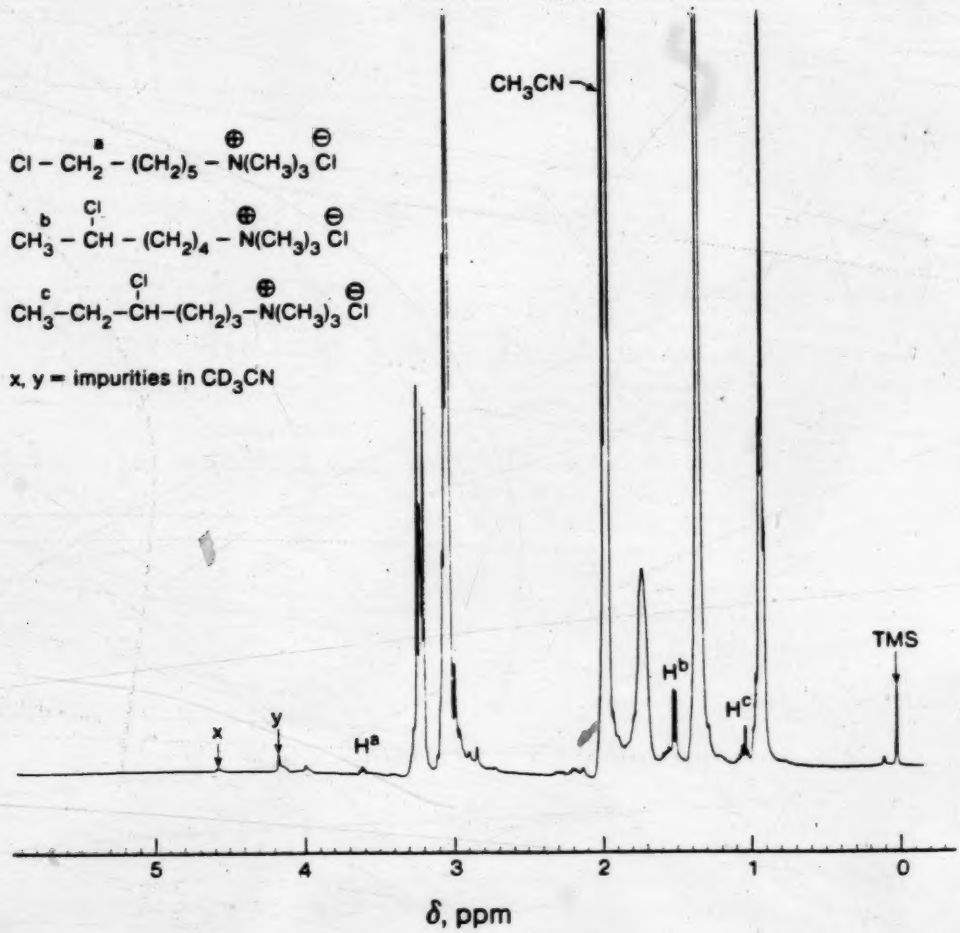


Figure 2. 400 MHz ^{1}H NMR Spectrum of the Reaction Product Mixture from the Photochlorination of n-Hexyltrimethylammonium Chloride with Molecular Chlorine in 15% CD_3CO_2D/85% H_2SO_4.

Appendix II. The Photobromination of Neopentane, Dichloromethane and Chloroform with NBS, 15°.

Reagent, M		Substrates, mmol			Reaction, %[a]	Mass Balance, %		
Additive	[NBS]/[Additive]	CH_2Cl_2	C_5H_{12}	$CHCl_3$	(Yield), %[b]	NS-	Br-	r
Ethylene	$0.10/1.1\times10^{-2}$	15.6	0.38	12.4	25.4 (32.2)	98.4	72.2	17.6
	$0.10/1.1\times10^{-2}$	15.6	0.38	12.4	46.6 (25.1)	109	90.8	11.6
	$0.10/1.1\times10^{-2}$	15.6	0.38	12.4	59.8 (23.9)	115	85.2	9.69
Bromine	$8.5\times10^{-2}/7.8\times10^{-4}$	15.6	2.14	12.4	18.0 (64.2)	105	41.6	0.086
	$8.5\times10^{-2}/7.8\times10^{-4}$	15.6	2.14	12.4	100 (62.2)	100	104	0.048

a. Based on percent conversion of NBS.
b. Percentage of products arising from chloroform, based on total abstraction products.

Appendix III. Derivations of Equations 52, 53 and 54.

Calculation of $X_{NS\cdot}$ (Equation 52)

The following symbols are used to simplify the expressions derived.

R = r_{obs}, the r value measured for mixed chain experiments

R_N = $r_{NS\cdot}$, the r value attributed to a pure succinimidyl radical chain

R_B = $r_{Br\cdot}$, the r value attributed to a pure bromine atom chain

$$Q = \frac{[C_5H_{12}]^o \times 6}{[CH_2Cl_2]^o}$$

N = $[C_5H_{11}Br]$, the total neopentyl bromide formed

D = $[CHCl_2Br]$, the total bromodichloromethane formed

N_N = $[C_5H_{11}Br]_{NS\cdot}$, the neopentyl bromide formed from succinimidyl

N_B = $[C_5H_{11}Br]_{Br\cdot}$, the neopentyl bromide formed from bromine atom

D_N = $[CHCl_2Br]_{NS\cdot}$, the bromodichloromethane formed from succinimidyl

D_B = $[CHCl_2Br]_{Br\cdot}$, the bromodichloromethane formed from bromine atom

$$R = \frac{N}{D \cdot Q} \qquad \text{(A) (the expression for the relative rate ratio observed)}$$

$$R_N = \frac{N_N}{D_N \cdot Q} \quad \text{(B) (the expression for the relative rate ratio for succinimidyl radical)}$$

$$R_B = \frac{N_B}{D_B \cdot Q} \quad \text{(C) (the expression for the relative rate ratio for bromine atom)}$$

$$N = N_N + N_B \quad \text{(D) (by definition)}$$

$$R = \frac{N_N + N_B}{D \cdot Q} \quad \text{(E) (substitution of D into A)}$$

$$N_N = R_N \cdot D_N \cdot Q \quad \text{(F) (rearranged B)}$$

$$N_B = R_B \cdot D_B \cdot Q \quad \text{(G) (rearranged C)}$$

$$N_N + N_B = (R_N \cdot D_N + R_B \cdot D_B)\, Q \quad \text{(H) (F + G)}$$

$$R = \frac{(R_N \cdot D_N + R_B \cdot D_B)Q}{D \cdot Q} \quad \text{(J) (substitution of H into E)}$$

$$R = \frac{R_N \cdot D_N + R_B \cdot D_B}{D} \quad \text{(K) (cancel Q's)}$$

$$D_B = D - D_N \quad \text{(L) (by definition)}$$

$$R = \frac{R_N \cdot D_N + R_B(D-D_N)}{D} \qquad \text{(M) (substitution of L into K)}$$

$$R \cdot D = R_B \cdot D + D_N(R_N - R_B) \qquad \text{(N) (rearranged M)}$$

$$D_N = \frac{D(R-R_B)}{(R_N-R_B)} \qquad \text{(O) (rearranged N)}$$

$X_{NS\cdot}$ = mole fraction of total products arising from succinimidyl radical abstraction

$$X_{NS\cdot} = \frac{N_N + D_N}{N + D} \qquad \text{(P) (by definition)}$$

$$X_{NS\cdot} = \frac{R_N \cdot D_N \cdot Q + D_N}{N + D} \qquad \text{(Q) (substitution of F into P)}$$

$$X_{NS\cdot} = \frac{D_N(R_N \cdot Q + 1)}{N + D} \qquad \text{(R) (rearranged Q)}$$

$$X_{NS\cdot} = \frac{(R-R_B)D}{(R_N-R_B)} \cdot \frac{(R_N \cdot Q + 1)}{N + D} \qquad \text{(S) (substitution of O into R)}$$

$$X_{NS\cdot} = \frac{(R-R_B)}{(R_N-R_B)} \cdot \frac{D(R_N \cdot Q + 1)}{N + D} \qquad \text{(T) (rearranged S)}$$

$$D = \frac{N}{R \cdot Q} \qquad \text{(U) (rearranged A)}$$

$$X_{NS\cdot} = \frac{(R-R_B)}{(R_N-R_B)} \cdot \frac{N(R_N \cdot Q + 1)}{(R \cdot Q)(N + N/(R \cdot Q))} \qquad \text{(V) (substitution of U into T)}$$

$$X_{NS\cdot} = \frac{(R-R_B)}{(R_N-R_B)} \cdot \frac{(R_N \cdot Q + 1)}{(R \cdot Q)\ (1 + 1/(R \cdot Q))} \qquad \text{(W) (cancel N's)}$$

$$X_{NS\cdot} = \frac{(R-R_B)}{(R_N-R_B)} \cdot \frac{(1/R \cdot Q)(R_N \cdot Q + 1)}{(1 + 1/(R \cdot Q))} \qquad \text{(X) (rearranged W)}$$

$$X_{NS\cdot} = \frac{(R-R_B)}{(R_N-R_B)} \cdot \frac{(RN/R + 1/R \cdot Q)}{(1 + 1/R \cdot Q)} \qquad \text{(Y) (rearranged X)}$$

$$X_{NS\cdot} = \frac{(R-R_B)}{(R_N-R_B)} \cdot \frac{(R_N + 1/Q)}{(R + 1/Q)} \qquad \text{(Z) (multiplication by R/R)}$$

substituting original symbols yields:

$$X_{NS\cdot} = \frac{(r_{obs.} - r_{Br\cdot})}{(r_{NS\cdot} - r_{Br\cdot})} \cdot \frac{(r_{NS\cdot} + Q^{-1})}{(r_{obs.} + Q^{-1})} \qquad (52)$$

Calculation of $[BrCHCl_2]_{NS\cdot}$ (Equation 53)

The same symbols are used as were defined in the derivation of equation 52.

$$R_N = \frac{N_N}{D_N \cdot O} \qquad (A)$$

$$D_N = \frac{N_N}{R_N \cdot O} \qquad (B) \text{ (rearranged A)}$$

T = the total brominated substrates formed (RBr)

$$N_N + D_N = (N + D)X_{NS\cdot} = TX_{NS\cdot} \qquad (C) \text{ (by definition)}$$

$$N_N = (T \cdot X_{NS\cdot}) - D_N \qquad (D) \text{ (rearranged C)}$$

$$D_N = \frac{(T \cdot X_{NS\cdot}) - D_N}{R_N \cdot O} \qquad (E) \text{ (substitution of D into B)}$$

$$D_N + \frac{D_N}{R_N \cdot O} = \frac{T \cdot X_{NS\cdot}}{R_N \cdot O} \qquad (F) \text{ (rearranged E)}$$

$$D_N \left(1 + \frac{1}{R_N \cdot O}\right) = \frac{T \cdot X_{NS\cdot}}{R_N \cdot O} \qquad (G) \text{ (rearranged F)}$$

$$D_N = \frac{(T \cdot X_{NS\cdot})/(R_N \cdot Q)}{1 + (1/(R_N \cdot Q))} \qquad \text{(H) (rearranged G)}$$

$$D_N = \frac{T \cdot X_{NS\cdot}}{(R_N \cdot Q) + 1} \qquad \text{(J) (rearranged H)}$$

substituting original symbols yields:

$$[BrCHCl_2]_{NS\cdot} = \frac{T \cdot X_{NS\cdot}}{(r_{NS\cdot} \cdot Q) + 1} \qquad (53)$$

:

Calculation of r (Equation 54)

The following symbols are used:

A = C_5H_{12}

B = CH_2Cl_2

S· = succinimidyl radical

The reactions involved are:

$$S\cdot + A \xrightarrow{k_1} \longrightarrow C_5H_{11}Br$$

$$Br^{\bullet} + A \xrightarrow{k_2} \longrightarrow C_5H_{11}Br$$

$$S^{\bullet} + B \xrightarrow{k_3} \longrightarrow CHCl_2Br$$

$$Br^{\bullet} + B \xrightarrow{k_4} \longrightarrow CHCl_2Br$$

$$S^{\bullet} \xrightarrow{k_5} \longrightarrow \beta\text{-BPIC (reversible ring opening is neglected)}$$

From these equations:

$$\frac{-dA/dt}{-dB/dt} = \frac{k_1[A][S\bullet] + k_2[A][Br\bullet]}{k_3[B][S\bullet] + k_4[B][Br\bullet]} \qquad (A)$$

If [A] and [B] do not change significantly during the reaction:

$$\frac{\Delta A/[A]}{\Delta B/[B]} = r' = \frac{k_1\int_o^t[S\bullet]dt + k_2\int_o^t[Br\bullet]dt}{k_3\int_o^t[S\bullet]dt + k_4\int_o^t[Br\bullet]dt} \qquad (B)$$

$$r' = \frac{k_1 + k_2\int_o^t[Br\bullet]dt/\int_o^t[S\bullet]dt}{k_3 + k_4\int_o^t[Br\bullet]dt/\int_o^t[S\bullet]dt} \qquad (C)$$ (division of top and bottom of B by $\int_o^t [S^{\bullet}]dt$)

note: r' = relative reactivity/molecule = 6 r

Now take into account that S• also yields ß-BPIC:

$$\frac{d[\text{ß-BPIC}]dt}{d[\text{Total Products}]/dt} = \frac{k_5[S\cdot]}{(k_1[A]=k_3[B]+k_5)[S\cdot]+(k_2[A]+k_4[B])(Br\cdot]} \qquad (D)$$

If Y = the final total yield of ß-BPIC per total products:

$$1/Y = \frac{k_1[A]+k_3[B]+k_5}{k_5} = \frac{k_2[A]+k_4[B]}{k_5} \cdot \frac{\int_o^t [Br\cdot]dt}{\int_o^t [S\cdot]dt} \qquad (E)$$

If Ys = the yield of ß-BPIC per total products for a pure S• chain under these conditions, then:

$$1/Ys = \frac{k_1[A] + k_3[B] + k_5}{k_5} \qquad (F)$$

$$\frac{\int_o^t [Br\cdot]dt}{\int_o^t [S\cdot]dt} = \frac{1/Y - 1/Ys}{\left(\frac{k_2[A] + k_4[B]}{k_5}\right)} \qquad (G) \text{ (substitution of F into E and rearrangement)}$$

$$r' = \frac{k_1+(k_2(1/Y-1/Ys)k_5/(k_2[A]+k_4[B]))}{k_3+(k_4(1/Y-1/Ys)k_5/(k_2[A]+k_4[B]))} \qquad \text{(H) (substituion of G into C)}$$

This demonstrates that how [S•] and [Br•] vary with time, is not important to the value of r'.

$$r' = \frac{(k_1/k_5)((k_2/k_4)[A]+[B])+(k_2/k_4)(1/Y-1/Ys)}{(k_3/k_5)((k_2/k_4)[A]+[B])+(1/Y-1/Ys)} \qquad \text{(J) (multiplication of top and bottom of H by } (k_2[A] + k_4[B])/k_4k_5)$$

substituting original symbols yields:

$$r = \frac{1}{6} \cdot r' = \frac{1}{6} \cdot \frac{(k_1/k_5)((k_2/k_4)[C_5H_{12}]+[CH_2Cl_2])+(k_2/k_4)(1/Y-1/Ys)}{(k_3/k_5)((k_2/k_4)[C_5H_{12}]+[CH_2Cl_2])+(1/Y-1/Ys)} \qquad (54)$$

Appendix IV. Error Analysis for Equation 54.

The equation used to calculate r is shown below:

$$r = \frac{1}{6} \cdot \frac{(k_1/k_5)((k_2/k_4)[C_5H_{12}]+[CH_2Cl_2])+(k_2/k_4)(1/Y-1/Ys)}{(k_3/k_5)((k_2/k_4)[C_5H_{12}]+[CH_2Cl_2])+(1/Y-1/Ys)} \qquad (54)$$

The rules for estimating the propagation of errors are:

1) Addition or subtraction

$$\Delta(X \pm Y) = |\Delta X| + |\Delta Y|$$

2) Multiplication

$$\Delta(XY) = |Y\Delta X| + |X\Delta Y|$$

3) $$\Delta(X/Y) = \frac{|X\Delta Y| + |Y\Delta X|}{Y^2} = \frac{|X\Delta Y|}{Y^2} + \frac{|\Delta X|}{Y}$$

The parameters used are:

$$k_1/k_3 = 114 \pm 10.2$$

$$k_2/k_4 = 0.336 \pm 0.042$$

$$k_3/k_5 = 2.087 \times 10^{-3} \pm 3.85 \times 10^{-4}$$

For a point taken from Table XVII the following data is used:

$r_{obs.} = 1.44$ $\quad$ ß-BPIC $= 0.042 \pm 0.0017$

$BrCHCl_2 = 0.015 \pm 2.3\times10^{-4}$ $\quad$ $C_5H_{11}Br = 0.016 \pm 2.4\times10^{-4}$

$[C_5H_{12}] = 1.96$ $\quad$ $[CH_2Cl_2] = 15.6$

$$\frac{1}{Y} = \frac{\text{ß-BPIC} + BrCHCl_2 + C_5H_{11}Br}{\text{ß-BPIC}} = \frac{(0.042\pm0.0017)+(0.015\pm2.3\times10^{-4})+(0.016\pm2.4\times10^{-4})}{0.042\pm0.0017}$$

$$\frac{1}{Y} = \frac{0.073 \pm 2.17\times10^{-3}}{0.042 \pm 1.7\times10^{-3}}$$ (addition of errors in the numerator)

$$\Delta\left|\frac{1}{Y}\right| = \frac{|0.073\times1.7\times10^{-3}|}{(0.042)^2} + \frac{|2.17\times10^{-3}|}{0.042} = 0.122$$

$$\frac{1}{Ys} = (k_1/k_5)[C_5H_{12}] + (k_3/k_5)[CH_2Cl_2] + 1$$

$$\frac{1}{Ys} = (114\pm10.2)(2.087\times10^{-3}\pm3.85\times10^{-4})(1.96) + (2.087\times10^{-3}\pm3.85\times10^{-4})(15.6) + 1$$

$$\frac{1}{Ys} = A + B + 1$$

$$\Delta A = |223 \times 3.85 \times 10^{-4}| + |4.09 \times 10^{-3} \times 10.2| = 0.128$$

$$\frac{1}{Ys} = (0.466 \pm 0.128) + (3.26 \times 10^{-2} \pm 3.85 \times 10^{-4}) + 1$$

$$\Delta\left|\frac{1}{Ys}\right| = 0.128 + 3.85 \times 10^{-4} = 0.128$$

$$\frac{1}{Y} - \frac{1}{Ys} = (1.74 \pm 0.122) - (1.50 \pm 0.128)$$

$$\Delta\left|\frac{1}{Y} - \frac{1}{Ys}\right| = 0.122 + 0.128 = 0.25$$

$$(k_2/k_4)[C_5H_{12}] + [CH_2Cl_2] = (0.336 \pm 0.042)\ (1.96) + 15.6$$

$$\Delta|(k_2/k_4)[C_5H_{12}] + [CH_2Cl_2]| = 0.042$$

$$k_1/k_5 = (k_1/k_3)(k_3/k_5) = (114 \pm 10.2)(2.087 \times 10^{-3} \pm 3.85 \times 10^{-4})$$

$$\Delta\left|\frac{k_1}{k_5}\right| = |114 \times 3.85 \times 10^{-4}| + |2.087 \times 10^{-3} \times 10.2| = 0.065$$

Substitution of all results and errors into eq. 54 yields:

$$r = \frac{1}{6} \cdot \frac{(0.238\pm0.065)(16.3\pm0.042) + (0.336\pm0.042)(0.24\pm0.25)}{(2.087\times10^{-3}\pm3.85\times10^{-4})(16.3\pm0.042) + (0.24\pm0.25)}$$

$$= \frac{1}{6} \cdot \frac{C + D}{E + F}$$

$$\Delta|C| = |0.238 \times 0.042| + |16.3 \times 0.065| = 1.07$$

$$\Delta|D| = |0.336 \times 0.25| + |0.24 \times 0.042| = 0.094$$

$$\Delta|E| = |2.087\times10^{-3} \times 0.042| + |16.3 \times 3.85\times10^{-4}| = 6.4\times10^{-3}$$

$$\Delta|C+D| = 1.07 + 0.094 = 1.16$$

$$\Delta|E+F| = 6.4\times10^{-3} + 0.25 = 0.26$$

$$r = \frac{1}{6} \cdot \frac{3.96\pm1.16}{0.27\pm0.26} = \frac{1}{6} \cdot G$$

$$\Delta|G| = \frac{|3.96\times0.26|}{(0.27)^2} + \frac{|1.16|}{0.27} = 18$$

$$\therefore r = \frac{1}{6} \cdot 14.7\pm18$$

or $r = 2.45\pm3$

APPENDIX V. NMR Method for Analysis of Succinimide and β-Bromopropionamide.

The product mixtures were analyzed by 200 MHz ^1H nmr spectrometry. The solvent signals (CH_2Cl_2 or $CHCl_3$) and substrate signal (neopentane) were suppressed by homonuclear decoupling to produce an acceptable signal to noise ratio. The experiments involved the collection of at least 40 scans with a 10 second delay between acquisitions to ensure complete relaxation of all product signals.

The T_1 values for the protons measured were generally found to be less than 3.5 seconds. For experiments where poor material balances were obtained, however, the T_1 values were found to be as long as 10 seconds.